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(Succeeding Vol. 38, 1919, the Journal of Cutaneous Diseases)

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VOLUME 3

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NUMBER 1

A CONTRIBUTION TO THE STUDY OF EPIDERMOPHYTON INGUINALE

NOTES ON AN INQUIRY INTO THE MORPHOLOGY OF THE CAUSATIVE FUNGI; A CLINICAL AND LABORATORY STUDY OF THIRTY-SEVEN CASES OF DERMAL SCALING

GROVER W. WENDE, M.D., AND KATHARINE R. COLLINS, M.D.
BUFFALO

The higher fungi were credited with being the causative factors in the production of human disease processes long before the recognition of the important rôle played therein by the lower fungi by Langenbeck, 1839; Schoenlein, 1839; Pasteur, 1862, and Koch, 1882. During the era in which the causal relationship of bacteria to human disease was being developed, interest lagged in regard to the etiologic importance of the higher fungi. Since 1900, the importance of the higher fungi in the production of pathologic states has received more attention and their etiologic rôle has been more clearly recognized. That the integumentary system is most often the site for their implantation and growth is obvious and is shown in the large number and variety of skin lesions due to them.

The findings of bacteriologists and dermatologists lead one to consider that a wide distribution of dermatologic lesions due to the higher fungi exists; that many different species are causative factors, and that certain clinical types of such lesions may be produced by species morphologically dissimilar. On the other hand, one is constrained to believe that skin lesions clinically dissimilar may be due to the same species of fungi which at times may be virulent, at other times inert; at times pathogenic, at other times saprophytic. Indeed, Sabouraud claims that a change of country frequently determines a change in virulence, so that a change in local environment may well cause a change in morphologic development. All this may account for the seeming discrepancies in the discussions of various authorities, for the lack of sharp-cut distinctions, and for an amount of indefiniteness and obscurity that has prevented proper appreciation and clear understanding of interesting and easily recognized skin lesions—lesions that fre-

quently are permanently eradicated with great difficulty, that often are chronically recurrent, and that actually are unsightly and annoying but not dangerous nor deforming.

Probably no group of skin lesions has recently excited greater interest and investigation than those produced by tinea fungi. In 1844, Gruby described two varieties of fungi in ring form—large spore and small spore. This observation remained many years forgotten until it was revived and verified by Sabouraud. While *Tinea trichophyton*—large spore—lesions are common in tropical and subtropical regions, they are apparently not so common in temperate regions. Castellani, in 1905, while in Ceylon, described a fungus from human skin lesions that he called *Trichophyton cruris*; the fungus was independently reported in France by Sabouraud in 1907, and was named *Epidermophyton inguinale*. Castellani¹ claims that, according to the laws of nomenclature, this fungus should be called *Epidermophyton cruris*. *Epidermophyton inguinale* differs from the other tinea in that it does not attack the hair or hair follicles and in that the color of the colonies on Sabouraud's medium is lemon or orange yellow.

Since the publication in this country of the papers by Ormsby and Mitchell,² and by White,³ we have been particularly interested in the skin lesions said to be produced by *Epidermophyton inguinale*. We have endeavored to determine: whether the lesions on the flat skin surfaces and those in the skin folds, that clinically are so different, are due to different varieties of the same fungus or to a single variety morphologically modified by the slightly different environment presented by the various sites; and, if due to a fungus, whether the fungus is a modified trichophyton or a modified epidermophyton.

SITE OF EPIDERMOPHYTON INGUINALE LESIONS AND DURATION

From the designation *Epidermophyton inguinale*, the inguinal region would be considered the most frequent site of the lesions, but the few observations made by us indicate that the skin lesions due to the epidermophyton may be found on any part of the body. Our observations corroborate the statement made by White in his report on a many times larger number that in the United States the inguinal region is not so frequently the site as are other parts. In all probability the name was given to this fungus because it was first recovered from lesions occurring in the inguinal region. In our small series we found epi-

1. Lancet 1:945 (May 1) 1920.

2. Ormsby, O. S., and Mitchell, J. H.: Ringworm of Hands and Feet. J. A. M. A. 67:711 (Sept. 2) 1916.

3. White, C. J.: Epidermophyton Infection, J. Cutan. Dis. 37:501 (Aug.) 1919.



Fig. 1.—Vesicles appearing in groups and blebs; slight desquamation; resembles pompholyx.

dermophyton lesions at the following sites: face, one case; axilla, one case; hands, one case; abdomen, one case; nates, one case; anus, two cases; groins, five cases; thighs, two cases; legs, four cases, and feet, eleven cases.

Our findings also seem to corroborate those of White in regard to sex, age and duration. The larger number of lesions were found in males; they occurred during the third and fourth decades; the duration was in periods of months rather than days or years. Our inquiry did not go into the possible relation of occupation or into the possible source of the infection.

APPEARANCE AND TRANSMISSIBILITY

In general, the appearance of the lesions in our series may be summed up as areas of scaliness varying in size from that of a split pea to 4 and 5 inches square or even larger. The lesions were more or less sharp in outline, with thickening of the epidermis without inflammation of adjoining tissue, although underneath the scales there was some redness. In those areas in which the skin was naturally moist, as between the toes, the epidermis was moist and soggy. The color of the lesions in the moist area was usually a dirty white while in the dry areas it was more or less gray, red or brown. Distributed through portions of the lesions deep seated vesicles were frequently seen; often at the inception of the trouble blebs strikingly resembling pompholyx were present. Itchiness and hyperhidrosis were present, while in the folds and moist areas an unpleasant odor, almost a bromidrosis, occurred. Occasionally the process seemed to be influenced by the season, being worse in summer, better in winter.

In none of our cases could it be determined that autoinoculation took place, although the larger number of patients had multiple lesions in widely distributed areas. In regard to the transmissibility of *Epidermophyton inguinale*—we have under observation four members of one family each presenting proved epidermophyton lesions. The father has had patches in the groin and on both plantar surfaces for eighteen years; the mother has had the same condition in the groins and on both plantar surfaces for seven years; one son has had the condition on both plantar surfaces as well as interdigitally for one year, and another son has had it for nine months in the same locations as his brother.

CASES STUDIED BY AUTHORS

In the plan of study cases were selected from the ordinary day's work and short clinical records made. Scales and scrapings were obtained from the various lesions and subjected to microscopic examination for the presence of spores and mycelia; if possible, some of the hairs present in the lesions were included. In cases showing spores



Fig. 2.—Distinct dirty, white, soggy, intertriginous desquamation and thickening; desquamation over plantar surface with deep-seated vesicles.

or mycelia an effort at identification of the fungi was made by means of cultures from the specimens obtained both in vitro and in vivo. In order to check the work and as controls and for differential study specimens were taken from similar lesions due to other known fungi and from lesions of similar character not caused by fungi.

Diagnoses.—All the cases selected for observation presented skin lesions showing scaling with or without vesication, with or without slight redness and with little or no itching. Our series consists of thirty-seven cases, of which these clinical diagnoses were made: acne, two cases; blepharitis, one case; callus, two cases; dermatitis herpetiformis, two cases; eczema, five cases; folliculitis agminate (Hartzell) or hyphomycetes granulorum (Schamberg), one case; epithelioma, one case; neurodermatitis, one case; pityriasis rosea, two cases; tinea capitis, eight cases; tinea cruris, one case; tinea trichophytina, three cases; epidermophyton inguinale, eight cases; not diagnosed, one case.

Of the twenty-one cases which clinically were diagnosed as due to fungi, nineteen were found to present spores or mycelia of which thirteen may be classed as epidermophyton inguinale. Of the eight cases clinically diagnosed as epidermophyton inguinale, the cultures showed six to be due to that fungus. One case diagnosed as eczema proved to be due to the epidermophyton. Of the three cases diagnosed as trichophyton, all were proved to be epidermophyton. The case not diagnosed was shown to be due to the epidermophyton. The case diagnosed as agminate folliculitis proved to be due to epidermophyton. In the case diagnosed as tinea cruris the laboratory reported negative findings. From this analysis the clinical recognition of epidermophyton inguinale lesions is fairly easy, although unquestionably frequently overlooked because the lesions so imitate other skin conditions that careful and more extended examination of the patient is not made with the possibility of epidermophyton as the etiologic factor in mind.

Cultural Characteristics of Epidermophyton Inguinale.—Sabouraud, using the culture medium that bears his name, asserts that the peculiar cultural characteristics of the cryptogam, *Epidermophyton inguinale*, which is but a representative of the trichophyton group, while not making the recognition easy, make it less difficult; he also states that the fungus is isolated with comparative ease. He says that its characters and differences may be classified under three heads: (a) original appearance, (b) rapid pleomorphic transformations, and (c) organs. In his descriptions he states, under the heading appearance, that the culture growths show a powdery surface radiating in form, the center being umbilicated and covered by an embossment of the culture growth, in color a grayish-yellow with an areola of citrin hue, and that these forms are reproduced on proof mediums. Under the heading pleo-

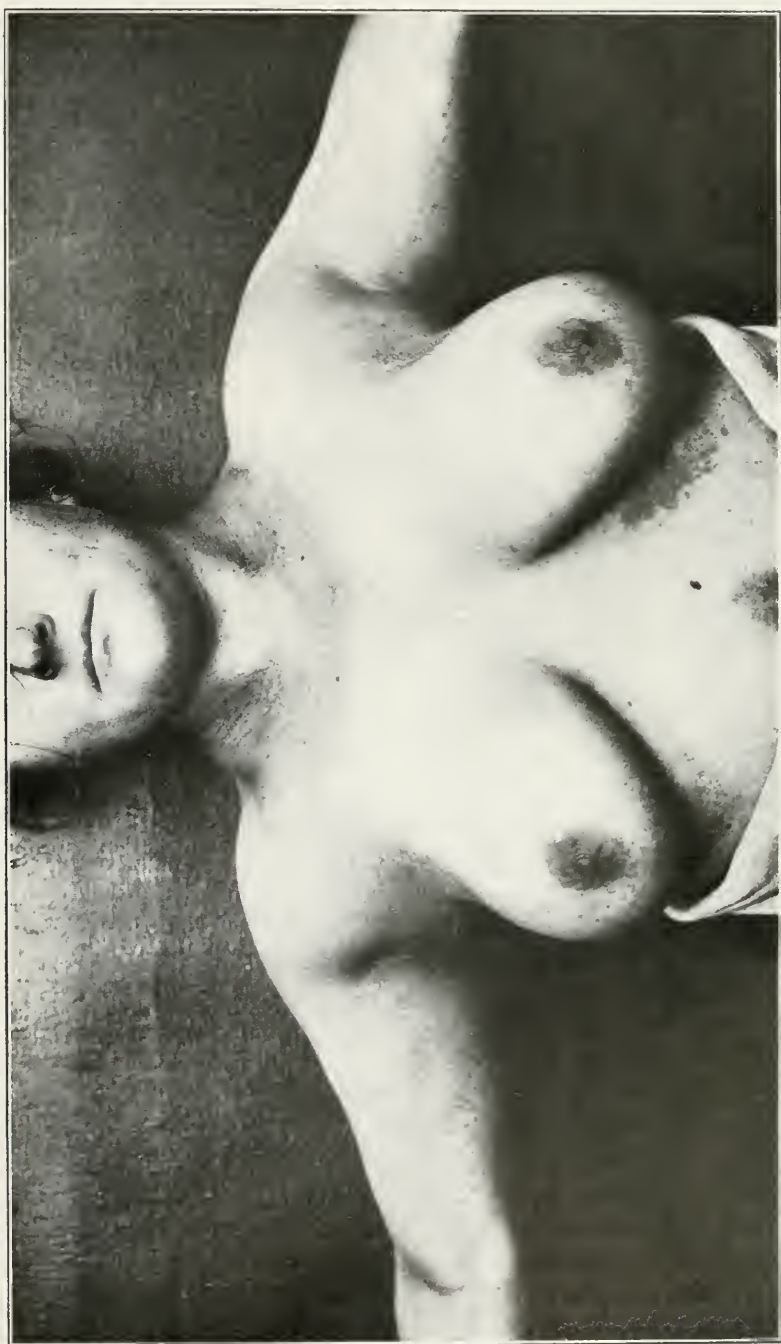


Fig. 3.—Large desquamating yellowish-brown areas on flat surfaces and in moist fields; history of vesication in axillae and under breasts. The condition has existed for twelve years; at times it has been almost absent, at others even more pronounced than shown. This case is not included in the thirty-seven systematically studied, but laboratory findings proved the presence of *Epidermophyton inguinale*.

morphism he says that the growth on sugar or glycerin mediums is especially characteristic of *Epidermophyton inguinale* in that after three or four weeks a white duvet of absorbent cotton-like tufts gradually covers the entire surface of the mediums; and that this degenerating form growth invariably is reproduced on reseeded in sugar mediums, while the original may be rejuvenated by planting in proof mediums like peptone water. Under the heading organs, he says that microscopically the growth presents enclosed clubs or asci, pediculated laterally or terminally on the mycelia filaments and usually arranged in banana-like bunches. Sabouraud further asserts that *Epidermophyton inguinale* is the only trichophyton cryptogam known to present these characteristics.

Technic Used by Authors.—Sabouraud's technic was followed throughout the laboratory study of the thirty-seven specimens examined. The investigation consisted of four steps: (a) the usual microscopic examination of the scales and hairs for spores, mycelial threads and fungal organs; (b) the direct making of two separate plants in Sabouraud's medium of the scales found to contain spores—these plants were designated "primary and secondary"—and the reseeded of each through ten to twelve generations which were designated "subsequent" cultures; (c) the microscopic examination of the mycelia and organs produced from each culture, and (d) the inoculation of guinea-pigs with the culture growth diagnosed as *Epidermophyton inguinale*. When an inoculation was made the hair of the guinea-pig was cut short, and the closely trimmed surface cleansed with alcohol and scarified, after which the macerated culture growth was rubbed in freely. As a control the hair was clipped at another location remote from the inoculation and the cut surface cleansed and scarified but not inoculated.

The stain used for the microscopic examinations from the first twenty-seven cases was methylene blue; for the remaining ten Ehrlich's triple-stain was used. In our opinion Ehrlich's stain gave the better picture.

The microscopic examination of the original scrapings from the thirty-seven cases showed the presence of spores in twenty-six, of mycelia threads in three and of fungal organs (asci) in five; spores were absent in thirteen cases.

Results.—The primary and secondary plantings of the twenty-six cases showing the presence of spores resulted in the production of fungal growths in twenty-four, while in two no growth was secured. The twenty-four molds were identified thus: *Epidermophyton inguinale*, 13; *Microsporon audouini*, 7; *Microsporon minutissimus*, 1; one unidentified mold; *Oidium*, 1 (later observation indicates that this was an epidermophyton); *Aspergillus*, 1 (the aspergillus was a common

contamination in most of our cases; this was corroborated in the animal inoculations; this fungus bears no relation to the etiology of the lesion. Most investigators report some type of the penicillium as a contaminating fungus; with us it was of rare occurrence).

Of the thirteen cases identified as *Epidermophyton inguinale*, the microscopic examination of the original specimens showed the presence of mycelium in three and of asci in five, spores in chains or rows in four and crescentic asci in five, one of which was also septated.



Fig. 4.—The various forms of mycelia and asci seen microscopically in the cultures of the epidermophytos, rubrum and citrin; 1, pyramidal asci; 2, fusiform and crescent asci.

The colonies in the upwards of 312 “primary and secondary” and “subsequent” cultures all showed a central acuminate growth surrounded by a distinct flattened areola which was again surrounded by the duvet as a lighter fringe; the only exceptions were those derived from one case in the colonies from which the areola was absent. In one case the areola was flat, an atypical growth; this case was off-type all the way through.

The characteristic pleomorphism was demonstrated in the matrass, which in all of the cultures was at first yellow or orange in color. This yellow color persisted in seven of the primary plantings and in four of the secondary plantings. In one both the primary and secondary plantings rapidly became rose red; this case seemed to answer to the description of the "*Epidermophyton rubrum*" of Castellani.¹ One case after several weeks in both primary and secondary plantings became green. In four cases of the primary plantings and in seven of the secondary plantings the matrass became black. In the subsequent cultures the same colors were respectively obtained as in the primary and secondary.

In all cultures the duvet began as an absorbent cotton-like growth, with the exception of one case in which the hyphae presented a



Fig. 5.—Forms of mycelia and asci seen microscopically in cultures of the epidermophytos, noire and noire-gris. The asci are tinted yellow to brown.

bristle-like growth and in one case in which the hyphae were short. The color of the duvet in all cultures at first was white. This persisted throughout in the red type and in the green type. In the yellow type after ten or twelve generations the duvet took on a salmon-pink color. In the black type the duvet passed through a grayish-green to a mouse-gray color, with the exception of one case in which it became soot black. Here also is evidence of pleomorphism.

In all cultures the mycelial threads were septated with occasional nonseptated, highly granular branches. The asci were given off terminally and laterally, often in bunches like bananas; they bore from two to eight or more spores. The mycelium in subsequent cultures was often a more or less homogeneous mass and not well differentiated as

to structure; the same condition was noted in two of the original specimens submitted; in the case in which the duvet became soot black the mycelial threads were clearly differentiated.

Except in two cases, pyramidal forms of asci were present in the primary and secondary plantings. In the seven black type cultures the pyramidal form persisted throughout all subsequent cultures. In the eight yellow type cultures, after a few generations, the pyramidal asci were lost. In twelve cases, fusiform, crescentic and oval asci occurred and were the pleomorphic forms. In the green type case only the oval asci were found. In one yellow type case the pyramidal forms of asci only appeared after the fourth reseedling to disappear in the following one. In seven cases of the red and yellow types the asci at times took on a diminutive form without change in character. One case, on the fourth reseedling, gave small spores, but in the following



Fig. 6.—Forms of mycelia, asci and spores seen microscopically in cultures of an atypical epidermophyton (laboratory case No. 8). The small slender mycelium and spores predominate. The asci are few in number.

ones reverted to large type. In the black cultures the asci took on yellow to brown tints.

The laboratory designation of "*Epidermophyton inguinale*" was based chiefly on the microscopic morphology. The pleomorphism in our series was marked and interesting, and a more careful and extended investigation should be made to account for it. Our systematic examinations were made on Sabouraud's medium. We used proof agar and beer-wort agar, but they did not give different results. All changes herein described took place in the same batch of mediums. Peptone

water was used for keeping the cultures. The formation of oxalate crystals in the medium was never noted in cases of the epidermophyton group, but was frequently observed in cultures of the penicillium and the aspergillus groups.

One interesting development in our work, which we believe has not been noted heretofore by other observers, is the presence of two types of the fungus in the same lesion. The two types gave identical skin reactions in the guinea-pig. Four of our cases showed this double infection.⁴

The inoculations into guinea-pigs with macerated pure cultures from each of the thirteen cases designated "*Epidermophyton inguinale*" gave rise to scaling in different degrees, and the hair did not grow in until after several weeks. Preparations of the scales from the inoculated

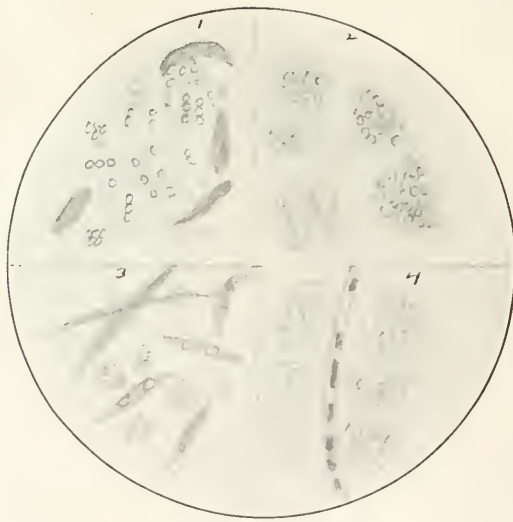


Fig. 7.—Microscopic appearance of scales treated with 30 per cent. potassium hydroxid and stained; 1, disintegrated scales—spores in rows and asci; 2, scales, slightly disintegrated, filled with spores; 3, scales, disintegrated, spores and asci and nondifferentiated mycelium; and 4, scales filled with spores and differentiated mycelium.

guinea-pigs showed mycelium and asci. The results from inoculations from both the black-gray type and the yellow type were identical. The findings were the same whether the two types had been isolated from the primary and secondary plantings from the same lesion or from the primary and secondary plantings which gave only one type. The pic-

4. In a recent personal communication from M. Sabouraud, he states that only one type is found in the same case and in the same lesion.—"Dans les cas de Trichophytie on ne trouve qu'une espèce sur un malade et jamais plusieurs Trichophytes sur un même malade et dans la même lésion."

ture presented in guinea-pig controls in which clipping and scarifying alone were done was very different; there was no scaling and the hair grew in quickly. In the guinea-pigs inoculated after the same manner with cultures of *aspergillus* the hair grew back in two days; there was no scaling. The guinea-pigs inoculated with *aspergillus* invariably died on the third or fourth day, whereas those inoculated with the "*Epidermophyton inguinale*" lived.

CONCLUSIONS

1. Recognition of the skin lesions of *Epidermophyton inguinale* presents little difficulty; these lesions occur relatively often among scaly skin diseases. Parts of the body other than the inguinal region present original lesions with greater frequency than the name would imply. This condition is well shown in Figure 3 in which there is a general distribution over the entire body; the lesions, however, are confined to the anterior surfaces and are found on the face extending down over the neck, in the axilla, over the shoulder down on the arm to below the elbow, on the trunk below the breasts, about the umbilicus, and on the toes; the groin lesions occurred as three slightly scaly areas, each about the size of a quarter. The designation is, therefore, somewhat misleading when considering lesions at other locations than in the groin.

2. *Epidermophyton* lesions vary so much in appearance that errors in diagnosis are easily possible unless reasonably full and careful clinical examination and study are made. The character of pleomorphism is as applicable to its lesions as it is to its laboratory growth; environment seems to affect the activity and character of both lesion and growth. In our cases the lesions of flat surfaces and of the folds were due to the same type of fungus.

3. The problems of autoinoculation, sources of infection and conditions favoring human implantation and growth should receive early study and solution, as the frequency of the disease indicates increasing virulence and possibly the development of greater pathologic importance.

4. Laboratory recognition is neither intricate nor difficult. It requires no apparatus not found in every modest clinical laboratory.

5. The characteristic appearance, pleomorphism and biologic reaction are readily secured, and are distinct and easily recognized. The conditions determining the pleomorphism should be further studied.

6. The multiplicity of laboratory growth types without apparent clinical pathologic variability has not before been reported. This presents an extremely interesting problem that should receive further investigation to determine whether it is of any etiologic value as well as mycologic importance.

TUBERCULOSIS OF THE LIP*

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Tuberculosis in the buccal cavity presents itself in almost as many diverse forms as on the integument, and frequently gives rise to diagnostic errors. The subject is given scant consideration in textbooks on dermatology, usually under the heading of tuberculosis cutis orificialis, and in books on general medicine it is considered briefly in relation to respiratory tuberculosis. Special treatises on diseases of the mouth, such as that of Mikulicz and Kümmell,¹ recognize these types of oral tuberculosis: (1) lupus of the mucous membranes; (2) tuberculosis ulcerations, rhagades and infiltrates of the tongue and lip; (3) isolated ulcers of the soft palate; (4) miliary ulcerations occurring at the corners of the mouth, on the lip and edges of the tongue in advanced cases of phthisis. Jadassohn,² in his masterly review of the subject of tuberculosis of the skin and mucous membranes, divides this into: (1) lupus of the mucous membranes; (2) miliary ulcerations involving the mucous membranes and adjacent skin; (3) tuberculous ulcers of nonmiliary character involving the lip, tongue and genital regions. Osler³ states that tuberculosis of the lip is extremely rare even in cases of advanced pulmonary disease. Considering the frequency with which tubercle bacilli in the sputum come in contact with the lips, it seems unusual that they should be so seldom affected. An internist who sees large numbers of pulmonary cases recently stated that he had never seen an involvement of the lip in more than 20,000 patients with tuberculosis examined by him. In view of these facts, the subjoined case seems of sufficient interest to warrant a detailed report.

* From the Department of Dermatology and Syphilology, Northwestern University Medical School.

1. Mikulicz, J., and Kümmell, W.: *Erkrankungen der Mundhöhle*, Ed. 2, Jena, 1911.

2. Jadassohn, J.: *Tuberkulose der Haut*, Mracek's *Handbuch der Hautkrankheiten* 4:1, 1907.

3. Osler, William: *Practice of Medicine*, Ed. 8, New York, D. Appleton & Co., 1912, p. 211.

REPORT OF CASE

History.—M. H., man, aged 56, presented himself at the Northwestern Medical School Dispensary complaining of a painful swelling of the lower lip. He gave a history of repeated attacks of pneumonia, the first one in 1890 in Russia, and again in 1902. Ten years ago, he had bronchitis and pleurisy. For many years he had had a winter cough, which had stopped three years before when he discontinued smoking. Recently he had had occasional night sweats, and had lost some weight. There was no history of hemoptysis. Ten months ago he first noticed the swelling of the lip which grew worse after influenzal pneumonia of three weeks' duration, in May, 1919. About the same time, ulcers in the mouth developed, causing pain and a burning sensation and difficulty in eating. He had had several teeth extracted in the last few months. His appetite was poor, and he complained of general weakness.

The family history was uneventful. Four sisters and one brother were living in Russia. His father died at the age of 68 of paralysis, and his mother



Fig. 1.—Tuberculosis of the lip. (The ulceration at the right is the biopsy wound.)

at 76 of senility. There was no family history of tuberculosis. One daughter and one son were in good health.

Physical Examination.—The patient was extremely emaciated and pale. Except for the chest findings, the physical examination was negative. Dr. Herbert W. Gray of the medical department made a careful examination of the chest and reported as follows: Distinct drooping of the right shoulder; very prominent clavicles on both sides, especially the right, on which side the fossae are very prominent; dull on percussion over both apices and over the first left interspace; hyperresonant over the second interspace and dull over the third and fourth on the same side; dull along both sides of the sternum from the first to the fourth interspaces.

Heart examination revealed the apex in the sixth interspace in the mid-clavicular line. The right border was 1.5 cm. left of the left parasternal line. There were two tones but no murmurs. Posteriorly the thorax was dull and hyperresonant, bilaterally from the apices down to the eighth rib and laterally to the midscapular line on the right and to the inferior border of the scapula on the left. The rest of the chest, particularly the right anterior and both

axillary regions, and inferiorly below the eighth ribs, was distinctly hyper-resonant to percussion with diminished breath sounds. There was compensatory breathing over both lower lobes in the axillary area. Distinct bronchial breathing of a cavernous character was noted at the apex of the right upper lobe. There was a difference of 1 cm. between forced inspiration and expiration, showing the high grade of emphysema present in the functioning lung. No râles were heard during the entire examination.

Diagnosis.—The diagnosis was chronic phthisis, with extensive chronic emphysema; heart displaced to the left due to pulling of adhesions; chronic mediastinitis; very slight degree of activity at the present time.

Roentgenologic Findings.—Dr. Blumenthal of the roentgen-ray department reported on the fluoroscopic examination as follows: extensive fibrosis of upper right lung; pericardial adhesions to the diaphragm; adhesions to the trachea displacing it toward the right; moderate fibrosis of the left lung.



Fig. 2.—Tuberculosis of the lip showing ulceration of the buccal mucous membrane.

Description of Lesions in the Mouth.—The entire lower lip was uniformly enlarged, about twice the size of the upper lip, and indurated to the touch, with several small areas of denuded epidermis. Under glass pressure, minute nodules could be discerned. The inner aspect of the lower lip down to the gingival border showed a superficially ulcerated area about 2 cm. broad with a granular base, sloping edges and was surrounded by edematous mucous membrane for some distance on each side. On palpation, the ulcer felt moderately indurated. At the inner aspect of the upper lip near the right commissure was an abruptly excavated ulcer 0.5 cm. in depth with an irregular base. This ulcer felt soft to the touch. Opposite the last lower right molar was a third shallow ulcer about 1 cm. in circumference of a similar type. The few remaining teeth in the lower set showed evidence of extensive decay and pyorrhea. The gums of the lower jaw were spongy, edematous, and exuded pus on pressure. The tongue, palate and pharynx appeared normal. A laryngologic examination was negative.

Laboratory Findings.—The Wassermann reaction was negative. The blood pressure was 115 systolic, and 65 diastolic. Hemoglobin was 75 (Sahli). Red blood cell count revealed 5,200,000 cells; the leukocyte count was 6,400. Differential count demonstrated: neutrophils 71 per cent., small mononuclears 22 per cent., large mononuclears 6 per cent., transitionals 2 per cent., basophils 1 per cent., eosinophils none. Urine examination disclosed: acid, specific gravity 1.018, faint trace of albumin, no sugar and no acetone. Microscopically, occasional hyaline casts were seen.

Diagnostic Comment.—The patient was exhibited at one of the meetings of the Chicago Dermatological Society, and the majority of the members expressed the opinion that the lesion of the lower lip was an epithelioma. The patient's age, the induration and the presence of a hard mass of glands in the submental region favored this diagnosis. However, the presence of a second ulceration near the angle of the mouth separated by an area of normal mucous membrane and of a third ulcer of the buccal mucosa was not entirely consistent with this view. Smears and scrapings were made from the ulcers in the mouth, stained with Ziehl's stain and showed large numbers of acid-fast bacilli—short thin rods of granular type, morphologically identical with tubercle bacilli. The diagnosis of tuberculosis of the lip with tuberculous ulcers of the mouth was further substantiated by the results of the biopsy. What appeared to be merely an edema of the lip proved to be a solid tuberculoma.

Histologic Examination.—Two pieces of tissue were removed for histologic study, one from the ulcer of the mouth and a wedge-shaped piece of tissue from the vermilion border of the lip. In addition to the usual stains, special stains for acid-fast bacilli were made. The lesion from the lip showed the epidermis to be normal or slightly thinned in part of the section, with the stratum granulosum intact. In other areas, there was extreme acanthosis, irregular down-growth of rete pegs, intracellular and extracellular edema of rete cells and infiltration with leukocytes.

The corium showed intense edema and dilatation of lymphatics and capillaries. Numerous cell masses were present in the middle and subpapillary layers. The cellular infiltration was composed of isolated and conglomerate tubercles of varying size with characteristic arrangement of giant cells, epithelioid cells and small round cells. Giant cells were numerous, oval or round, with ten to twenty peripherally arranged nuclei corresponding to Langhans' type. There was a tendency to conglomeration of tubercles around the vascular channels with an inflammatory zone around the cell groups. There was no tendency to coagulative necrosis of the center of the tubercles as seen in lupus. The collagen was edematous and stained poorly with eosin. The blood vessels were dilated with swollen endothelium. Ziehl's stain showed scanty numbers of tubercle bacilli in the corium. The histologic examination of the lesion from the floor of the mouth showed absence of the epidermis, a diffuse cellular invasion of the corium with relatively few giant cells and no definite arrangement into tubercles, but large numbers of acid-fast bacilli, many of them in clumps.

Treatment and Subsequent Course.—The patient was placed on a general tuberculous regimen, a high protein diet and cod-liver oil internally. Locally a cocaine ointment was used on the lip to relieve the pain, and the ulcers in the mouth were swabbed several times daily with diluted hydrogen peroxid. Filtered Coolidge treatments were administered over the lip and submental region. In

the course of six weeks, the swelling of the lip had diminished appreciably in size, and the ulcerations in the mouth had healed. The patient had gained in weight, but his general condition was still poor, and after several months he disappeared from observation.

GENERAL REVIEW OF THE SUBJECT OF TUBERCULOSIS OF THE LIP

The occurrence of tuberculous ulcers of the mouth and lips of the miliary type in advanced cases of phthisis has been known for a long time through the observations of Jarisch,⁴ Chiari⁵ and especially Kaposi.⁶ Among more recent reports of cases involving the lips are those of Plichon,⁷ Schuchardt,⁸ Morestin,⁹ Thibièrge, Hallopeau and

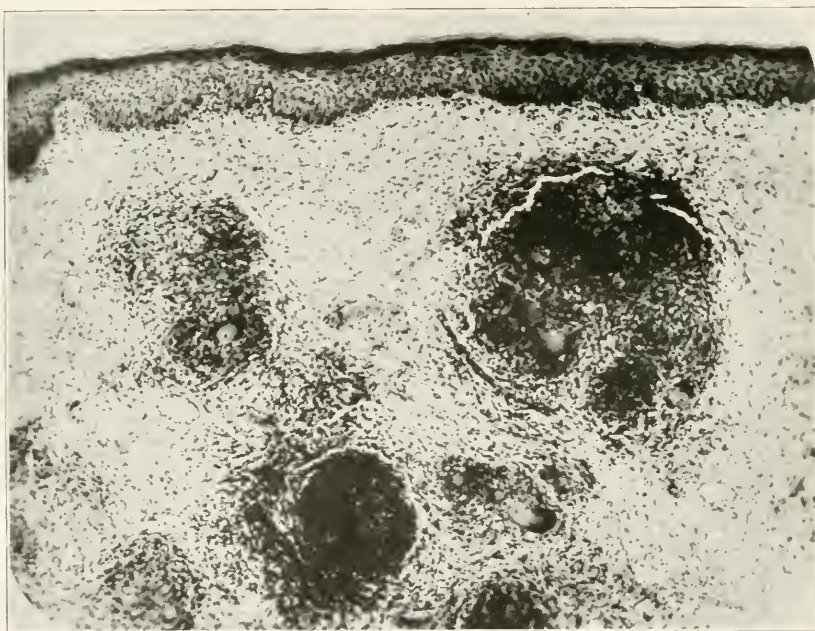


Fig. 3.—Low power photomicrograph showing isolated tubercles in the corium.

Ribot,¹¹ Münter¹² and others. These cases have been reported under various titles, as tuberculosis cutis vera, tuberculosis ulcerosa, tuber-

4. Jarisch: *Arch. f. Dermat. u. Syph.*, 1879, p. 265.
5. Chiari: *Arch. f. Dermat. u. Syph.*, 1879, p. 269.
6. Kaposi: *Arch. f. Dermat. u. Syph.* **43**:373, 1898.
7. Plichon, M.-E.: *Tuberculose des lèvres*, Paris, 1888.
8. Schuchardt: *Deutsch. med. Wehnschr.* **15**:1073, 1889.
9. Morestin: *Bull. et mém. Soc. anat. de Paris* **79**:108, 1904.
10. Thibièrge: *Ann. de dermat. et syph.* **8**:286, 1897.
11. Hallopeau and Ribot: *Ann. de dermat. et syph.* **13**:611, 1902.
12. Münter: *Berl. klin. Wehnschr.* **49**:1495, 1912.

culosis cutis orificialis and tuberculosis miliaris. The disease is confined to the mucous membrane and skin about the mucous outlets. Kaposi, in his series of twenty-two cases, found the cutaneous part of the lip involved in eight and the mucosa in six. The clinical characteristics of tuberculous ulcers of the miliary type are well known. They are shallow, round or oval in outline, with a pale red base covered with a seroviscid secretion and irregular borders showing miliary nodules. Tuberculous ulcers of the mouth and lips are further characterized by their rapid development, occasional destructive tendency and acute pain. It is rare to see the grouped miliary nodules before they break down. Ulcers form in from three to eight days and spread either deeply or superficially, simulating the breaking down of a gumma or carcinoma. The prognosis is usually grave as most patients are in the terminal stages of tuberculosis. Kaposi found that the outlook was not hopeless in every case, as the ulcers may show a tendency to heal after a certain stage is reached.

Tuberculous ulcers of the mucous membrane of nonmiliary type are not so well known and have been emphasized especially by Jadassohn,² Miyahara,¹³ Danlos¹⁴ and others. They are atypical, torpid, poorly granulating papillary ulcerations with undermined or heaped-up borders and resemble lupus ulcers. They are more chronic in their course and occur in association with visceral tuberculosis of a less fulminating type. A special variety is called by Jadassohn the chancreform or epitheliomaform type on account of its firmer consistency and the close resemblance to chancre or epithelioma. These tuberculous lesions occur on the lips as the result of exogenous inoculation in certain instances, and are analogous to the tuberculous ulcers of the genitalia, resulting from infection through ritual circumcision, and those around the fingers and nails occurring as a result of accidental inoculation from tuberculous material. In two cases of lesions on the lower lip, Jadassohn was not able to exclude the diagnosis of epithelioma until the histology was studied and tubercle bacilli were found. Miyahara has reported in detail a lesion on the vermilion border of the lower lip in the form of an indurated plaque, 1.5 cm. in diameter. Histologically he found small, sharply defined tubercles in the upper corium along the vein walls and around the lymphatics. Bacillary findings as well as guinea-pig inoculations were positive. A nodule in the cheek also showed a tuberculous structure and was regarded as a lymphogenous metastasis. There were no tuberculous lesions demonstrable elsewhere in the body, and the case was regarded as probably

13. Miyahara: Arch. f. Dermat. u. Syph. **111**:305, 1912.

14. Danlos: Bull. Soc. franç. de dermat. et syph. **10**:12, 1899.

the result of exogenous inoculation. The second case was a chancri-form tuberculosis of the lip in a child of 9 years. On the middle of the upper lip was a crust-covered ulcer, 0.5 by 3.25 cm., with some infiltration. Excision showed tuberculous structure with sparse bacilli. Later the child died of pulmonary and meningeal tuberculosis. Danlos, Münter and others have also reported tuberculous ulcers of the lip which resembled chancre. Many of the cases reported in the literature (Fleming, Bamberger, Paget, Spitzer, etc.) have been mistaken for epithelioma on account of the firm consistency of the border and base and the granular surface of the ulceration. The case here reported resembled more the epitheliomaform type of Jadassohn and was rather unusual in that it represented a solid tuberculoma of the entire lower lip with ulcerations of the buccal mucosa.

The pathogenesis of tuberculous lesions of the lip as well as other portions of the mucous membrane presents several possibilities. There may be a local infection of the lip from without, as in Miyahara's case, and a dissemination to other organs from this source. A rare possibility is a simultaneous infection of the mucous membrane and other viscera. The most probable mode of infection is a primary respiratory infection with secondary involvement of the lip by auto-inoculation or hematogenous infection. The lesion of the lip represents in most instances a direct infection of the tissues through a fissure or break in the mucous membrane. In the case here reported, the presence of carious teeth and infected gums in the lower jaw gave a clue to the possible mode of entrance of the bacilli. The extraction of teeth has been known to be followed by mucous membrane tuberculosis and involvement of the alveolar process and regional lymph glands.

The diagnosis of tuberculosis of the lip rests largely on the clinical characteristics of the ulcers, the absence of the cartilaginous induration of most chancres and epitheliomas, the negative spirochete examination and the presence of acid-fast bacilli in smears or scrapings. When bacilli are not found, a biopsy will settle the diagnosis. In the milary ulcerations the histologic picture will show chronic granulation tissue with few giant cells and an abundance of bacilli. The nonmilary type has a histology resembling Boeck's milary lupoid with sharply defined tubercles in the middle and upper corium with bacilli in scanty numbers. The typical arrangement of central giant cells, epithelioid and small round cells is found in these cases, whereas cheesy degeneration is absent. Guinea-pig inoculations may also be made in doubtful cases.

The treatment of tuberculous ulcers of the mouth includes the general treatment of the visceral infection, local use of antiseptic mouth

washes and local anesthetics for the relief of pain. Fifty per cent. lactic acid has been recommended as a cauterizing agent. Curetting or excision might be resorted to in favorable cases. The roentgen-ray and Finsen light have also been used. The prognosis depends on the extent of the visceral involvement.

CONCLUSIONS

1. The case here reported represents an unusual instance of solid tuberculoma of the lower lip with ulcerations of the buccal mucosa associated with a chronic pulmonary tuberculosis of the fibroid type.
2. Tuberculosis of the lip must be differentiated from chancre and epitheliomatous ulcerations.
3. A positive diagnosis rests on the finding of tubercle bacilli and the characteristic histology.

XVII.—EPITHELIOMAS DEVELOPING ON LUPUS ERYTHEMATOSUS

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While the development of epitheliomas on lupus erythematosus has been reported by a number of writers, it has always been with emphasis on the rarity of this condition. Four cases of carcinoma on lupus erythematosus, appearing on the service from which the subjects of these studies are drawn, should be added to those so far reported. Because of the nature of a skin and cancer clinic, where these patients, with the exception of one, presented themselves because of carcinoma, any conclusions as to the frequency of carcinoma on lupus erythematosus must be of questionable value. During the past ten years, 110 cases of lupus erythematosus appeared, including the four of this report, making the incidence of the occurrence of carcinoma on lupus erythematosus 3.6 per cent. at this clinic.

In an excellent exposition, Pringle¹ refers to previous reports of cases. His own report, however, is most complete.

From the chronicity of lupus erythematosus and the prolonged irritation from treatment, one might expect the resulting continuous trauma to lead to frequent development of carcinoma on such a favorable base. Wolbach has shown, in his work on carcinoma after roentgen-ray dermatitis, that a period of from eight to ten years is required for the development of carcinoma, and that the principal change is primarily vascular. All traumas when sufficiently prolonged are potentially a carcinoma stimulus, so that lupus erythematosus with its years of chronic inflammation is, therefore, a field containing potential carcinoma and should be so considered.

Possibly because a patient has for years reconciled himself to, or acquired a tolerance for, the personal discomfort of a chronic lupus erythematosus the added appearance of epithelioma fails, for some time at least, to arouse him to seek further relief, and in many cases the condition goes on to a fatal ending without further diagnostic differentiation. We must conclude from cases already reported and

* Studies, reports and observations from the dermatological department of the Barnard Free Skin and Cancer Hospital and the School of Medicine, Washington University, St. Louis, Mo., U. S. A., service of Drs. M. F. Engman and W. H. Mook.

1. Pringle: Multiple Epitheliomas Developing on Lupus Erythematosus, *Brit. J. Dermat.* **12**:1 (Jan.) 1900.

from those in this report, that multiple epitheliomas, with a rapid spread of the cancerous disease when on a lupus erythematosus base is the rule, and that the prognosis is not promising; also that factors before mentioned—the attitude of the patient, failure of proper differential diagnosis and rather rapid fatality—probably tend to prevent more frequent notation of the occurrence of this condition.

REPORT OF CASES

CASE 1 (Fig. 1).—N. H., aged 82, a white woman, was first seen Nov. 10, 1917. At that time she gave a history of lupus erythematosus for the past



Fig. 1 (Case 1).—Extensive lupus erythematosus scarring and carcinomatous lesion.

twelve years. The entire face was covered with the resulting scar. Four or five months ago a small pimple appeared on the right cheek, near the angle of the mouth. This soon showed signs of growing, according to the patient. Now there is a deep ulcerated lesion about 0.5 cm. deep and 4 cm. in diameter, with a well defined, nodular, pearly border. The glands of the neck are much involved.

Because of the patient's age and generally poor physical condition she was treated with the roentgen ray only. There was no improvement when the patient passed from supervision Dec. 7, 1917. She died Dec. 25, 1917 (cause unknown).

CASE 2.—H. B., aged 60, a white man, gave a history of lupus erythematosus beginning twenty-five years ago on the left cheek. He said it did not "trouble or bother" him much until recently, and after he had applied blue vitriol. At



Fig. 2 (Case 3).—Epithelioma on lupus erythematosus.

this time, May 17, 1915, examination showed an erythematous scarred lesion on left cheek 2.5 cm. wide and 5 cm. long. There was some crusting and scaling within the lesion, and where the scales were raised, small projections were seen extending down into the follicles. No positive carcinomatous lesions were observed. Treatment consisted of salicylic and zinc oxid salves, with recommendation for roentgen-ray treatment for which the patient failed to return.

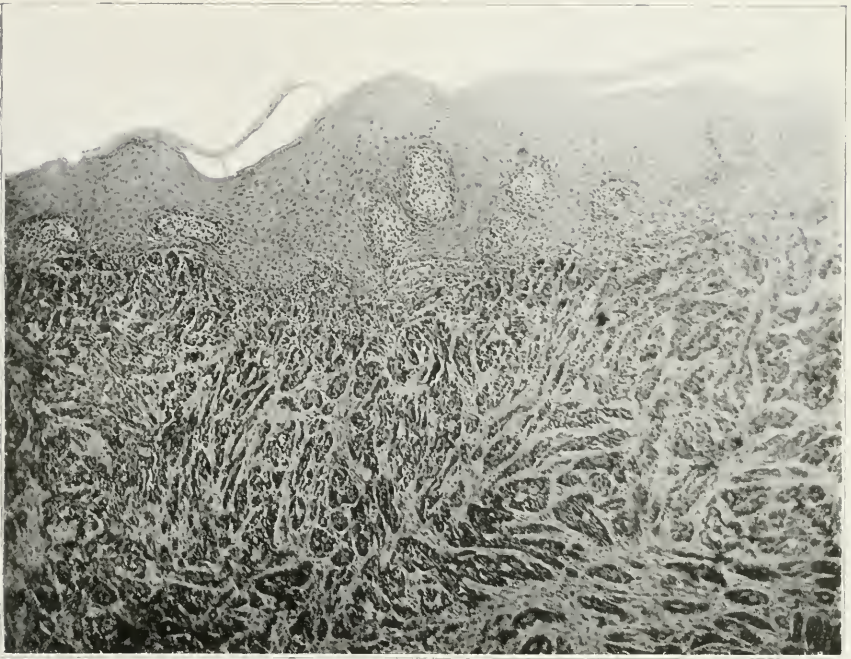


Fig. 3.—Low power section from Case 3.



Fig. 4.—High power section from Case 3 at beginning of cancerous area.

On June 6, 1919, the patient returned to the radium clinic in answer to follow-up cards. He had been using only local treatments of various salves. There was now a red, smooth scar, with numerous small pearly nodules along the border, evidently epitheliomas. The patient was given one radium application and then disappeared from our observation.

CASE 3 (Fig. 2).—T. D., aged 60, a white man, was treated May 29, 1908, for a lupus erythematosus on the face. He gave a history of twenty-four years' duration of the disease and insisted that it began in a razor cut. The patient did not return again for several years. On Feb. 9, 1915, he again



Fig. 5 (Case 3).—Numerous recurrences.

reported, and at this time the whole of the left cheek was involved in an eczematous ulceration, which was undergoing epitheliomatous degeneration and had destroyed part of the left ear. An ulcer at the angle of the left jaw was distinctly of the rodent ulcer type. There were some senile keratotic lesions on the right cheek and on the backs of both hands. The patient was treated with roentgen ray and at intervals with applications of Lassar's paste, xeroform and silver nitrate salves. There appeared to be slow but gradual improvement. Oct. 14, 1915, the lesion was curetted and skin grafted successfully. The microscopic diagnosis of the curettement was: basal cell carcinoma of the face.

Dec. 8, 1916, the wound had healed with the exception of a very small ulcer on the skin.

On Oct. 24, 1918, the patient again returned after a considerable lapse of time. There were now two ulcers on the left lower lip 4 mm. in diameter, several minute ulcers on the left temple and one behind the right ear, about 3 mm. in diameter. In the anterior part of the old scar there was an ulcerated area with rolled edges and irregular nodular floor, measuring from 2.5 cm. below the mucocutaneous margin of the lower lip, down on the midline of the neck to the thyroid cartilage and from the midline of the neck 4 cm.



Fig. 6 (Case 4).—Epithelioma on lupus erythematosus.

to the left. This the patient says has "gradually grown from a small scab." The glands on the right side of the neck were palpable. The patient was again referred for roentgen-ray treatment. Up to Dec. 9, 1918, there was no improvement; the ulceration measured 5 by 10 cm. on the neck and under the chin. The edges were sharp, nodular and pearly. Caustery and radium treatment appeared to effect some improvement. Improvement progressed so that the patient stayed away for a period of nearly eleven months.

On Nov. 10, 1919, he was again seen and at this time biopsy again brought out a diagnosis of basal cell carcinoma of the face. Figures 3 and 4 are microphotographs of sections made at this time. Microscopically these show the

lesion to be typical basal cell carcinoma. In the scar area, where no cancerous tissue is found, the section shows only an atrophic cicatricial condition; there is marked increase of fibrous connective tissue in the corium with total disappearance of all normal follicular or glandular structure. The epidermis shows a rather wider than normal stratum granulosum, though all the cells are not well defined and have large deeply staining nuclei, showing only a slight tendency to keratinization. The papillary layer between the epidermis and corium is wholly lost.

As one approaches the carcinomatous area there is an irregularity and thickening in the basal cell layer; at the edge of the carcinoma the irregularity of arrangement of the basal cells increases and there are papillary down-growths that show clearly the infiltrating character of the carcinoma. There is increased vascularity with some small round cell infiltration about this area of new growth induced, no doubt, largely by the active process of necrosis in the center of the lesion rather than being primary or coincident only to the new growth.

When last seen this patient showed numerous recurrences and metastases (Fig. 6).

CASE 4.—W. D., aged 41, a white man, has had lupus erythematosus for the past twenty-four years, involving the butterfly area of the face. Following injury to the nose by a tree branch two months ago, the patient noticed growth beginning at the site of the injury. At this time examination of the patient showed typical lupus erythematosus scarring on the nose and cheeks, and on the ridge of the nose there was a verrucous appearing lesion, raised about 6 mm., and its size was about 3.5 by 2.5 cm. The edges were sharply limited with a nodular pearly border.

The patient was given radium application, and on May 25, 1920, there was apparently a complete disappearance of the cancerous lesion.

ERYTHEMA NODOSUM AND TUBERCULOSIS

REPORT OF A CASE TERMINATING IN TUBERCULOUS MENINGITIS,
WITH NECROPSY

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In 1914, Foerster¹ summarized the literature on the association of erythema nodosum with tuberculosis, laying special emphasis on the association of the cutaneous picture with miliary tuberculosis in childhood. He mentioned in particular the reports of Pollak,² Dunlop,³ Abt,⁴ and Sezary,⁵ of patients who had died of tuberculous meningitis in close sequence to an attack of erythema nodosum. Such a clinical sequence implies a hematogenous distribution of tuberculosis bacilli; and yet the outstanding fact of the literature has been the failure of the majority of efforts to demonstrate the presence of bacilli by inoculations either from the blood stream or the tissue of the nodose lesions. Of the numerous investigators who have attacked this problem only Brian,⁶ Hildebrandt,⁷ and Landouzy⁸ claim positive results.

Schönfeld's⁹ study of thirteen cases of tuberculids, undertaken under Zieler's¹⁰ direction, secured only negative results. It was impossible to obtain the bacilli from the blood stream or to demonstrate

1. Foerster, O. H.: The Association of Erythema Nodosum and Tuberculosis, *J. A. M. A.* **63**:1266, 1914.

2. Pollak, R.: Erythema nodosum und Tuberkulose, *Wien. klin. Wchnschr.* **25**:1223, 1912.

3. Dunlop, J.: Erythema Nodosum and Tuberculosis, *Brit. Med. Jour.* **2**:120, 1912.

4. Abt, I. A.: Erythema Nodosum, *J. A. M. A.* **43**:1454, 1904.

5. Sezary, A.: Erythème noueux et méningite tuberculeuse, *Gaz. d. hôp.* **85**:125, 1912; Erythema Nodosum and Tuberculous Meningitis, *Med. Press & Circ., N. S.* **94**:32, 1912.

6. Brian, O.: Untersuchungen über die Aetiologie des Erythema nodosum, *Deutsch. Arch. f. klin. Med.* **104**:272, 1911.

7. Hildebrandt, W.: Zur Aetiologie des Erythema nodosum, *München. med. Wchnschr.* **54**:310, 1907.

8. Landouzy, L.: Erythème noueux et septicémie a bacilles de Koch, *Presse méd.* **21**:941, 1913.

9. Schönfeld, W.: Experimentelle Untersuchungen zur Frage des Vorkommens virulenter Tuberkelbazillen in der Blutbahn bei Hauttuberkulosen nach diagnostischer Tuberkulinanwendung und unter anderen Bedingungen, *Arch. f. Dermat. u. Syph.* **126**:651, 1919.

10. Zieler; Demonstration, Fall 13, *München. med. Wchnschr.* **61**:450, 1914; Vorstellung, Fall 3, *ibid.*, p. 1480.

their presence by inoculation. Schönfeld refers to Zieler's case, an abstract of which follows:

REPORT OF CASES

ZIELER'S CASE.—A girl, aged 24, with no clinical signs of tuberculosis, came under Zieler's observation July, 1913; she had a high fever and an acute erythema nodosum. From this attack she made a good recovery, but in September of the same year a tuberculous nodule appeared in the skin of the left eyebrow and a scrofuloderma-like lesion on the tip of the nose. For another three months the patient remained in excellent health. She then began to complain of backache. Simultaneously pulmonary signs of tuberculosis appeared, the patient became febrile and March 15, nine months after her erythema nodosum, she died of miliary tuberculosis. Necropsy showed that the miliary dissemination had occurred about three weeks before death. A large number of blood inoculations and 400 serial sections from the tissue of a nodose lesion failed to demonstrate the tuberculosis bacillus by the methods of Ziehl and Much.

The patient observed by me supplies further clinical evidence, though no conclusive proof, for the belief that erythema nodosum may in some cases be of purely tuberculous etiology.

CASE 259600.—A young girl, 19 years of age, came to the clinic complaining of an eruption over the shins and knees associated with rheumatism so severe she could scarcely walk. The process was of one week's duration. To the date of first examination the lesions had shown no tendency to the usual involution with color changes.

The patient gave a definite history of exposure to tuberculosis in the person of an older sister who had recently died of the disease. The patient herself had always been well until the week during which the nodose lesions appeared. Since then she had lost weight and had a cough for two weeks with no expectoration and no fever.

At the time she presented herself her afternoon temperature was 100. The physical examination of the chest and the roentgenogram were negative, the urine was normal, and the serum Wassermann reaction was negative. A search for a clinically demonstrable focus of septic infection was negative. The appendix had been removed four years before and the tonsils three years before. There were no palpable glands, and the teeth were normal except for a slight pyorrhea. One feature of the erythema nodosum which deserves special note is its failure to show the usual hemorrhagic changes and the peculiar purplish or bluish tinge of the individual nodes and plaques.

Under rest in bed and the administration of salicylates the patient made a definite improvement and was dismissed with instructions to continue medication and to return later for observation.

Twenty-two days after the patient's first examination and twenty-nine days after the first appearance of the erythema nodosum she developed a stiff neck, and in rapid succession the symptoms of a fulminating tuberculous meningitis appeared. Death occurred seven days later, thirty days after the onset of the erythema nodosum. Examination of the spinal fluid one day before death showed that the Wassermann and Nonne reactions were negative; there were forty-two lymphocytes and tuberculosis bacilli in small numbers. Necropsy disclosed an extensive recent miliary tuberculosis involving all the viscera.

including the myocardium, with a primary focus apparently in the peribronchial lymph nodes. A careful study of the tuberculous process showed the oldest lesions to be of approximately three to four weeks' duration. No signs of a septic focus of any description could be found in the entire body.

Histopathologic examination of a bluish patch over one of the tibiae showed the essential lesion to be in the muscle and to consist apparently of a simple necrosis with practically no evidence of inflammatory reaction. The tissue could not be stained successfully for tuberculosis bacilli, but nothing to suggest the histologic architecture of a tuberculous process could be identified.

DISCUSSION

The outstanding features of interest in this case are:

1. Absence of clinical evidence of tuberculosis when the patient presented herself with rheumatoid symptoms and erythema nodosum.
2. The apparently exact correspondence of the onset of erythema nodosum with the time of generalization of the tuberculous infection as estimated by the age of the tubercles found at necropsy.
3. The complete absence both in life and at necropsy of the septic foci responsible for erythema nodosum of the streptococcal or Rose-now¹¹ types.

It may not be amiss to suggest that one of the reasons why attempts to isolate the tuberculosis bacillus from the blood of patients with tuberculids and erythema nodosum are so conspicuously unsuccessful in spite of the strong clinical evidence for hematogenous distribution, is the time at which such inoculations are attempted. The moment at which the tuberculous bacteremia is at its height may reasonably be expected to precede the appearance of the lesions that give the clue to the condition by several days or even longer. The investigator who attempts to demonstrate the organism by blood inoculation into animals during the febrile stage of erythema nodosum is probably too late. The febrile reaction represents the response of the body to tuberculosis bacilli securely lodged in the tissue rather than still at large in the blood stream. The conclusive demonstration of a tuberculous bacillemia must depend on the opportunity to use a large number of animals in the study of a single patient suffering from recurrent attacks of a tuberculid in which the possibility of a pyogenic focal element has been entirely eliminated. The difficulty in securing such a combination of circumstance and opportunity will probably long delay the conclusive demonstration of the tuberculous etiology of certain types of erythema nodosum. In the meanwhile, the search for organisms should be directed toward the earliest recognizable lesion rather than toward mature lesions in which the inflammatory reaction perhaps has destroyed the bacterial embolus.

11. Rosenow, E. C.: The Etiology and Experimental Production of Erythema Nodosum, *J. Infect. Dis.* **17**:367, 1915.

STUDIES ON ALBUMINURIA AND EOSINOPHILIA IN SCABIES *

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PHILADELPHIA

The association of albuminuria with scabies has been a matter of interest, speculation and investigation for over a hundred years. Although it would seem that so simple a matter could be easily and finally settled, yet the results of investigation by different authors vary greatly, not only as to its frequency and severity, but even to its actual occurrence.

LITERARY REVIEW

Posner¹ found albumin in the urine of all scabies patients with his reagent. Spiegler, quoted by Hubner, also came to the same conclusion; but Hubner² showed that these observers had used a reagent that gave a positive reaction from dilutions of 1:50,000 at least, and for which, as even Spiegler himself remarked, it was difficult to find albumin free controls. The reagent was also positive with peptone albuminoses and nucleo-albumins. Hubner found albumin in the urine of forty-seven out of fifty scabetic patients with Spiegler's reagent, but in only two with the ordinary clinical tests.³ He believed that clinical tests would show an albuminuria in scabies patients only when there was some "circulatory cause," such as infection or fever.

Probably the most extensive series of cases reported was that by Nicholas and Jambon,⁴ who found albuminuria in sixteen out of 101 untreated cases with the ordinary clinical reagents. It appeared only after the disease had lasted for some time—one to two months or more in their cases. They, with Hubner, also insisted on some "predisposing factor," namely, a special sensitiveness of the kidneys so that the slightest irritation sufficed to bring on the condition.

The scabic albuminurias, according to Nicholas and Jambon, may be divided into two classes: (1) a slight transient albuminuria generally improving when sulphur treatment is begun, and usually much

* From the Laboratory of Dermatological Research, Department of Cutaneous Medicine, University of Pennsylvania.

1. Posner: *Virchows Arch. f. path. Anat.*, 1886, p. 114.

2. Hubner, H.: *Ztschr. f. klin. Med.* 1904, p. 549.

3. We have not been able to locate the formula for Posner's reagent. That of Spiegler's is as follows: HgCl_2 , 8 gm.; tartaric acid, 4 gm.; glycerin, 20 gm.; water, 290 gm. In applying the test, acidulate the urine with acetic acid, filter and overlay with the above reagent.

4. Nicholas and Jambon: *Ann. de dermat. et syph.* 9:65, 1908.

diminished or even disappearing in twenty-four hours; (2) a true "nephrite scabique" showing all the clinical signs of a real nephritis in contradistinction to a simple albuminuria. The latter condition occurred in two of their sixteen cases; at least one patient gave a definite history of having had an acute nephritis before. The past medical history of the other was not clear. Albuminuria did not seem to be dependent on the severity of the infestation, but when it occurred it was always in generalized cases. The presence of pustules did not have much influence, for only five of their fourteen cases of albuminuria showed them.

AUTHORS' STUDIES

Our data are based on the examination of forty-nine patients. Practically all were uncontrollable outpatients, so that consistent repeated examinations were not practicable.

Some of the cases as usual were complicated by the suppuration of secondary infection. At the time of urinalysis thirty-five of the forty-nine patients had not yet received treatment. The remaining fourteen had received three or four sulphur rubs on four consecutive nights, with the exception of two patients who will be referred to later. In collecting urine the usual care was taken to avoid contaminating discharges. The tests used were the three common clinical ones, i. e., acetic acid and heat, nitric acid, and Roberts' reagent.

As regards the whole series of forty-nine cases, albumin was found in ten, 20.4 per cent. Of these the urine in only one case showed a cloud, and this was light. The other nine cases showed a "very faint trace," i. e., albumin could be seen only when the tubes were held in the most advantageous position and light. Albuminuria was equally divided between males and females. The latter patients' ages ranged between 3 and 20 years, and 50 per cent. of the patients were under 10 years of age.

Of the thirty-five untreated patients, six showed albumin, 17.1 per cent. In the fourteen treated patients, four showed albumin, 28.5 per cent. The medicinal history of these four was that two had had sulphur rubs for six consecutive days (at their own instance), one had been taking a patent "blood medicine" and the fourth had taken three sulphur rubs and was using a phenol wash. In all cases (five) in which subsequent urinary examinations were made, the albumin had promptly disappeared.

Of the patients showing albumin, all had a generalized eruption of the hands, arms, legs and trunk. None showed any special or peculiar type of lesion, nor were pustules especially in evidence. In fact they were more conspicuous by their absence.

Therapeutic measures appear to increase the incidence of albuminuria. Thus in our series the percentage jumped from 17.1 per cent. (without treatment) to 28.5 per cent. when sulphur rubs were employed. With other authors it has even proved serious. Thus Thibierge⁵ reports that 95 per cent. of the patients treated with "Dutch soap" (Schmierseife) showed albuminuria. Lassar⁶ reports a death from the use of petrolatum over the entire body for four successive days. The patient developed an acute nephritis with edema. Of 124 patients rubbed with styrax, Unna⁷ reported definite kidney irritation in nine cases. Balsam of Peru will also produce albuminuria when used even in therapeutic amounts, according to Litten⁸ and Hubner.

TABLE 1.—THE OCCURRENCE OF ALBUMINURIA ACCORDING TO DIFFERENT OBSERVERS

Observer	Reagent Used	Number of Patients Examined	Percentage Showing Albumin
Posner.....	Posner's	...	100
Spiegler.....	Spiegler's	...	100
Hubner.....	Spiegler's	50	94
	Clinical*	50	4
Nicholas and Jambon.....	Clinical	101	16
Hayman and Fay.....	Clinical	49	20.4

* By clinical reagents is meant acetic acid and heat, or nitric acid.

TABLE 2.—SHOWING DISTRIBUTION OF ALBUMINURIA (AUTHORS' SERIES)

	Number of Patients Examined	Males	Females	Number Showing Albumin
Untreated.....	35	21	14	6— (17%)
Treated.....	14	11	3	4— (28%)

In our series albuminuria was slight and transient in all but one case. Hyaline casts were occasionally present in one case. In no case were the urinary findings of clinical significance, and the patients complained of only cutaneous symptoms.

ANIMAL EXAMINATION

We have also examined the urine from three dogs which were "spontaneously" infested with sarcoptic mange. None had received treatment. The first dog was not as seriously affected as the others, and had lost only about one-half of his hair. He did not show albumin at any time. The second dog had been diseased for about

5. Thibierge: *Ann. de dermat. et syph.*, 1895.

6. Lassar: *Virchows Arch. f. path. Anat.* **72**:132, 1878.

7. Unna, quoted by Hubner.

8. Litten, quoted by Hubner.

four months and had little hair left; at first his urine showed no albumin. A month later, when very weak, his urine was constantly cloudy with albumin. The third dog was also very sick and had little hair left. His urine showed albumin constantly. These findings will be commented on later.

CAUSE OF THE ALBUMINURIA

Four possible causes are: (1) a secondary pyogenic infection, (2) the therapeutic measures employed, (3) a preexisting nephritis, and (4) the disease itself.

1. We believe that secondary infection is unimportant since albuminuria occurred independently of pustulation in 100 per cent. of our cases.

2. Therapeutic measures undoubtedly produce albuminuria in some cases, as shown by the higher incidence we obtained in treated cases (23 against 17 per cent). However, Nicholas and Jambon found albumin in 16 per cent. of their untreated cases, and our series showed its presence in 17 per cent.; hence therapeutic measures are not invariably the cause of "scabic albuminuria."

3. Albuminuria occurs in too large a percentage of cases (16 per cent.) to assume that it is always the manifestation of a preexisting nephritis; one-sixth of our dispensary patients do not harbor nephritis. Furthermore, it is too transient to indicate a genuine nephritis. In the more severe cases, however, the "nephritis scabique" of Nicholas and Jambon, a preexisting nephritis, seems more than probable. This condition did not occur among our patients, and of the two cases recorded by Nicholas and Jambon at least one gave a definite history of a previous nephritis.

4. That albuminuria is a manifestation of the disease itself is the opinion of Nicholas and Jambon. They advance four possible factors: suppression of the skin function, toxins of the parasites, resorption of products from cells detached from the skin lesion, and vasomotor disturbances in the kidneys of reflex origin, due to irritation of peripheral nerves at the skin lesions.

We believe that the first three factors may reasonably be eliminated as immediate and exciting causes. The fact that albuminuria occurs in dogs, in whom the excretory functions of the skin are either absent or limited to a small amount by way of the sebaceous glands, points against the suppression of the skin function as a cause of albuminuria. It also seems improbable that it is due to any toxin of the itch mite, for there are too many generalized and long standing cases of scabies that show no albuminuria. The possible absorption of products from detached cells in the cutaneous lesions seems too fanciful to consider

as the burrows are almost without exception in the horny layer of the epidermis where absorption is difficult; also there are great numbers of detached cells on normal skins at all times.

That irritation of the cutaneous nerve ends may cause a reflex hyperemia or inflammation of the kidney is hard to prove but, on the whole, it seems to us to be the most plausible explanation. According to Herbert French,⁹ albuminuria occurs in various vasomotor disturbances, such as Raynaud's disease, angioneurotic edema and also occasionally in pemphigus. We appreciate, of course, that in some of these a secondary toxic or infectious factor enters which explains the albuminuria. Along the same lines, Adami¹⁰ calls attention to the fact that irritation of nerve ends may cause a reflex hyperemia or even a reflex inflammation in another part of the body, when this part is supplied by nerves that leave the cord at the same level as those that are irritated enter it.

In applying this principle to the scabic problem and referring to the nervous connections between the skin and the kidneys, we find that:

1. The nerves to the kidney are derived from the renal plexus.
2. The renal plexus in turn receives contributions from (a) the aortic plexus, (b) the solar plexus and (c) the least splanchnic nerve.
3. As far as peripheral cutaneous communication with the last three are concerned, they are limited to (a) the aortic plexus, between the tenth and the eleventh dorsal ganglions; (b) the solar plexus, from the ganglions between the fifth and ninth dorsal segments and from the right vagus; (c) the least splanchnic from the twelfth dorsal ganglion.

An inspection of these peripheral communications shows that all are truncal, and not immediately with the extremities in any case except one. This peripheral communication is the one from the right vagus, which gives a cutaneous branch to the right cervical region (which scabies does not attack, and with which we are therefore not concerned). This observation shows first, that sufficiently direct communications obtain between the skin and kidneys to make a reflex hyperemia possible; secondly, it links up suggestively with our findings that the albuminuria in our series of cases occurred only in generalized cases; that is, in cases in which the trunk is involved. Cases limited to the hands and arms, in which there were numerous

9. French, Herbert: *Index of Diagnosis*, New York, William Wood & Co., 1918.

10. Adami: *Textbook of Pathology*, New York, Macmillan Co., 1918, p. 84.

lesions of long standing and considerable inflammation of the parts, showed no albumin, while 20 per cent. of the cases with a generalized eruption, even if there were few lesions on the trunk, showed albuminuria.

Reflex irritation best surmounts the apparent impasse of why albuminuria appears in some generalized cases and not in others, even when the conditions appear identical, for it is reasonable to suppose that some economies are more sensitive to reflex reactions than others. We realize that speculative conclusions are on the whole generally unsatisfactory, and we make these statements as a theory rather than as a finality.

IMPORTANCE OF ALBUMINURIA

Although the presence of albuminuria in scabies is of considerable scientific interest and the method of its production a fruitful field for thought and experiment, it can hardly be of clinical importance. It is generally known that a simple albuminuria without the presence of casts occurs under a great variety of circumstances—exposure to cold, severe exertion, a heavy meal rich in proteins, etc. Such albuminurias, together with those that are accidentally discovered in young men in apparently robust health, which disappear after rest in bed and are not constantly present, are generally classed as psychologic, functional or accidental. We believe that the albuminuria of scabies belongs to this group.

CONCLUSIONS

1. A slight transient albuminuria occurred in 17.1 per cent. of the untreated scabies cases in our series. It occurred only in generalized cases. Probably, as suggested by Nicholas and Jambon, some special predisposing kidney irritability is present in these cases.
2. There is no evidence that an actual nephritis or kidney irritation of any clinical significance is produced by the disease itself. If such a condition occurs, it must be exceedingly rare.
3. The use of even mild therapeutic measures greatly increases the incidence of albuminuria, and some measures may lead to serious results.

EOSINOPHILIA

The presence of a slight but definite eosinophilia in scabies is much better established than albuminuria, although not accepted by every one. Kolmer,¹¹ in a series of eighteen children, found a mild leukocytosis, and an eosinophilia varying from 3 to 11 per cent. Two thirds of the cases reached 5 per cent. or over and the average for the series was 5.79 per cent. Noninfested children of the same age showed

11. Kolmer, J. A.: *Jour. Cutan. Dis.* 1911, p. 339.

2.73 per cent. of eosinophils. The eosinophilia was in general proportional to the severity of the infestation, was highest during the acme of the eruption, and gradually reached normal proportions as the disease disappeared.

Schamberg and Strickler,¹² in the examination of the blood of forty-seven scabetic patients, found that thirty-eight, or 80 per cent., showed 5 per cent. or more of eosinophils. The maximum count was 19 per cent.

Ewing¹³ comments that the various cutaneous diseases have furnished some of the most marked and interesting examples of eosinophilia. It has been shown by Canon¹⁴ and verified by Zappert¹⁵ that the eosinophils are affected not so much by the special forms of the cutaneous lesions as by the extent, intensity and lack of healing tendency of the lesions.

Herbert French,¹⁶ after the study of the blood in ninety patients with various skin diseases, dissents from the generally accepted statement that eosinophilia is common in various acute and chronic cutaneous disorders. He found eosinophilia only thirteen times in the ninety patients, and in only four cases was it marked. In his seven cases of scabies the average eosinophil count was only 1.6 per cent., the highest 6.6 per cent. and the lowest 0.1 per cent.

TABLE 3.—SHOWING GROUPING OF CASES ACCORDING TO PERCENTAGE OF EOSINOPHILS

Eosinophils	Number of Cases	Percentage of Total Number of Cases
3% or less	12	21.8
3-5%	11	20.0
5-7%	12	21.8
7-10%	17	30.9
10% or more	3	5.4
Total	55	99.9

We have examined the blood of fifty-five scabies patients in the dermatologic dispensary of the University Hospital and in the dermatologic wards of the Philadelphia General Hospital. Thirty of the patients were males and twenty-two females, and the ages ranged from 3 to 30 years. Our counts gave a maximum of 15 per cent. and a minimum of 1 per cent; the average was 5.5 per cent. Table 3 shows how the percentages were grouped. Thirty-two cases, or 58

12. Schamberg and Strickler: *Jour. Cutan. Dis.* **30**:53, 1912.

13. Ewing: *Clinical Pathology of the Blood*, Philadelphia, Lea & Febiger, 1918.

14. Canon: *Deutsch. med. Wchnschr.* **18**:206, 1892.

15. Zappert: *Ztschr. f. klin. Med.* **23**:227, 1893.

16. French, H.: *Guy's Hospital Rept.* **58**:81, 1904.

per cent., showed 5 per cent. of eosinophils or more, while twenty of these, or 36.6 per cent. of the series showed 7 per cent. of eosinophils or more. The higher percentages came from more extensive infestations, the low or normal counts either in very recent cases, in which symptoms had been noted for only two or three days, or else in light infestments. The presence of pustules did not seem to be a factor. The eosinophilia increased with the extent of the disease and disappeared promptly as the disease was cured.

The observation of Leredde,¹⁷ that in dermatitis herpetiformis and the various forms of pemphigus there is not only a hemic eosinophilia but an enormous outpouring of these cells into the cutaneous lesions, prompted the question whether this occurred in scabies also. We determined the eosinophil percentage of blood drawn from a finger and that from the neighborhood of a burrow or papule in five patients. The average difference was 0.3 per cent. In two cases the percentages were the same; in one the hemic (finger) count was less, and in two it was slightly greater. The difference is thus too slight or variable to be of any importance.

CONCLUSIONS

1. Scabies is accompanied by a slight but definite eosinophilia, the degree of which is, in general, proportional to the extent of the infestation.

2. There is no increase of blood eosinophilia in the neighborhood of the cutaneous lesions.

3. Being so variable in itself and so common in other skin conditions, eosinophilia is not useful in the differential diagnosis of scabies.

17. Leredde: *Prat. dermat.* **2**:527, 1902; *Ann. de dermat. et syph.*, 1898, p. 1016; *Monatschr. f. prakt. Dermat.* **27**:381, 1898.

PITYRIASIS RUBRA PILARIS

REPORT OF A CASE CURED BY THYROID EXTRACT

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INTRODUCTION

It is our desire and purpose to report a case of pityriasis rubra pilaris (Devergie) apparently cured by the internal administration of thyroid substance. Thyroid substance has been advocated therapeutically in this disease by several authorities; therefore when the patient, whose history is reported, appeared for treatment, it was decided to employ organotherapy in view of certain minor signs of dysthyroidism. With the exception of a 2 per cent. salicylic acid ointment used at the onset for a period of two days, no further measures, either general or local, were employed. We are further emboldened to report this case by reason of the rapid involution occurring, soon after the glandular medication was begun, in a disease generally regarded as pursuing a protracted clinical course and as being unusually resistant to all forms of treatment, either internal or local.

REPORT OF CASE

History.—B. B., a white man, married, aged 61, a native of Russia, a shirt-maker, presented himself in April, 1919, for the treatment of an intensely pruritic eruption. He said that the cutaneous condition began four months prior to his admission to the clinic with a mild itching of the skin of the abdomen. Four days later, a scaliness of the skin of the trunk was noticed which spread rapidly, involving the face and upper extremities, until at the end of ten days, it became generalized. The pruritus was so intense that it interfered with sleep and prevented him from attending to his occupation. Subsequently, the skin became dry, rough and cracked, and about three months after onset, the soles and palms were similarly involved. The condition persisted, steadily growing worse, and treatment received from clinics and private physicians gave no relief.

Inquiry showed that no other member of his family had suffered from any generalized or chronic skin disease, nor was any history of carcinoma, syphilis, tuberculosis or blood dyscrasia to be elicited.

The patient had been married forty years. He denied venereal infection by name or symptom; he had always been well with the exception of the diseases of infancy and childhood and a recurrent winter cough of several years' duration.

His wife was healthy; she was the mother of five children, all living and well. Her labors had been normal and she had had no miscarriages.

General Examination.—The patient was below normal stature, fairly well nourished but poorly developed, and showed difficulty in concentration and a faulty memory. His hair was thin, dry, lusterless and gray. His eyes revealed a marked arcus senilis; the eyelashes were scant; the eyebrows were sparse with the outer halves missing. The teeth were in poor condition; some were missing and the remainder were carious, yellow and showed extensive pyorrhea. The thyroid gland was not visible, nor could it be felt on palpation. The chest was barrel shaped; expanding poorly on inspiration. The spine showed moderate dorsal kyphosis and lumbar lordosis. The lungs revealed small, dry râles scattered throughout both areas. The cardiovascular system showed evidence of poor tone. The heart sounds were weak; a systolic murmur was heard at the apex and not transmitted. The pulse was small and easily compressible; the rate was slow, varying between 60 and 66 beats per minute. The superficial arteries were thickened, distended and sclerotic. Varicose veins were present on the legs and in the scrotum. The pubic hair was of the male type. The Wassermann reaction was negative. The urine was normal with the exception of a trace of albumin (repeated analyses). Biopsy was not permitted.

Dermatologic Examination.—The entire cutaneous surface was dry, scaly and thickened. Covering the whole skin area were innumerable, red, acuminate papules produced by hyperkeratosis in the mouths of the pilosebaceous follicles, which imparted to the touch a rough nutmeg grater-like sensation. Movements of the patient or rubbing of the skin caused showers of fine bran-like scales. The scalp was red and buried under a thick layer of grayish white scales. The hair was dry, lusterless and projected from hard, dark red papules. The skin of the face was red, dry, thickened, moderately scaly and showed the presence of groups of black, follicular papules over both malar regions. The skin of the trunk was also dry and scaly. The characteristic follicular papules were discrete but in places, as over the epigastric and sacral regions, they had also become confluent to form large, red, infiltrated, lichenified, slightly scaly, eczematoid patches. Scattered over the back were about a dozen large pea-sized lesions. These were elevated, covered with dirty, grayish scales and resembled nummular psoriasis. However, these patches differed from those of psoriasis, in that the scales were not of the silvery white color but of a dull, dirty, grayish appearance and when removed showed no bleeding points nor an underlying bright red surface, but a dry, livid, red base.

The skin of the extremities showed the same general characteristics, the eruption being most marked on the extensor surfaces. Psoriasiform lesions were present on both arms and legs, while large eczematoid patches covered the buttocks and thighs.

On the dorsum of the fingers, especially over the proximal phalanges, there were numerous discrete, hard, black, acuminate papules pierced by broken off

hairs and covered with scales. The palms and soles were the sites of a marked tylosis. The epidermis was greatly thickened, hard, almost horny in places, and covered with a thick, dense layer of dirty yellow and grayish scales. The hyperkeratosis extended up the lateral aspects of the hands and feet, being bordered by a narrow erythematous zone. The nails of the fingers and toes were dry, thickened, brittle and discolored. In the regions of the joints were deep, red fissures.

Course and Treatment.—Since pityriasis rubra pilaris is essentially a hyperkeratosis, an ointment containing salicylic acid, 2 per cent., in petrolatum was prescribed in an endeavor to reduce somewhat the thickened, horny layer. Furthermore, it was decided to administer organotherapy because of previous good results obtained with such measures in other keratodermias, especially ichthyosis.¹ Whole thyroid gland tablets, in 1 grain strength, were prescribed three times daily before meals. At the end of two days, the ointment was discontinued in order to demonstrate and test more thoroughly the efficiency of the thyroid medication without any local assistance. Within a week, an improvement was noticed, shown in a diminished tendency to scaling; new papules did not seem to develop so readily and the older papules, as well as the erythematous patches, had become flatter and less inflammatory.

A note made two weeks after instituting the treatment indicates that the improvement was distinct. Pruritus was slight and the follicular papules were less in number, many having disappeared, while the whole cutaneous surface was smoother and less nutmeg-grater like in character. The scaling was also less abundant; 75 per cent. of the characteristic black acuminate papules had disappeared from the dorsum of the fingers, and the eczematoid patches were less inflammatory and infiltrated.

The patient was presented at a regular meeting of the Manhattan Dermatological Society about three weeks after the treatment was begun and although the clinical picture had altered, it was still sufficiently characteristic to be accepted as an example of pityriasis rubra pilaris.

Under no treatment but that described, improvement continued until at the end of three months the skin showed no positive lesions of the disease, appearing only dry and slightly scaly. The scalp, however, continued to show a thin layer of dry grayish scales.

On request, the patient returned for examination one year after his first visit to the clinic. The skin appeared normal except for a slight seborrhea of the scalp. He stated that he had been taking the thyroid tablets on and off since his discharge from the clinic because of their good effect, not only on his skin, but also on his general condition, both physical and mental.

OTHER REPORTS ON THE THERAPEUTIC ACTION OF THYROID IN PITYRIASIS RUBRA PILARIS

There are several references in the literature concerning the effect of thyroid gland medication in pityriasis rubra pilaris.

Crocker² found the administration of thyroid extract a valuable adjuvant to local treatment. He recommended an initial daily dose

1. Forchheimer: *Therapeuses of Internal Diseases*, New York, D. Appleton & Co. 1:76.

2. Crocker: *Diseases of the Skin*, Philadelphia, P. Blakiston's Son & Co. 1:235.

of 5 grains with a weekly increment according to the tolerance of the patient; he asserted that it was rarely necessary to exceed fifteen grains daily until the cure was effected.

Graham Little³ reported good results in one case by the administration of thyroid extract in doses of $1\frac{1}{2}$ grains increasing to 3 grains, three times daily. Local treatment was employed simultaneously.

In Stelwagon's⁴ case thyroid extract seemed of slight service, but as the external treatment was being carried out at the same time, it was doubtful to which the benefit was due.

Pusey⁵ classifies thyroid extract, pilocarpin and protiodid of mercury as remedies that have seemed to be of benefit in some cases.

Ormsby,⁶ Sequeira⁷ and Sutton⁸ quote the article by Crocker regarding the internal administration of thyroid extract.

In Allbutt and Rolleston's "System of Medicine,"⁹ thyroid extract is mentioned as being tried, with temporary improvement in a few cases.

Schamberg¹⁰ recommends arsenic, mercury, pilocarpin, thyroid extract and tonics as internal remedies to be considered.

Whitfield¹¹ states that thyroid extract especially has been found of service, but in conclusion remarks that in his own experience nothing is of the slightest benefit and a case of his was unaltered by any form of treatment that has been recommended.

COMMENT

A review of the findings in this case demonstrates the presence of symptoms of hypothyroidism, and the rapid improvement under thyroid therapy warrants a belief that dysthyroidism may play a rôle in the production of pityriasis rubra pilaris. The thyroidal indications presented were: a dull, stupid facial expression with mental changes of a minor character; marked evidence of senility; sparseness of the eyebrows and absence of the outer half (Leopold-Levi and H. de Roth-

3. Little: *Brit. J. Dermat.* **22**:412, 1900.

4. Stelwagon: *Essentials of the Skin*, Philadelphia, W. B. Saunders Company, p. 235.

5. Pusey: *Principles and Practice of Dermatology*, New York, D. Appleton & Co., p. 446.

6. Ormsby: *Diseases of the Skin*, Philadelphia, Lea & Febiger, p. 337.

7. Sequeira: *Diseases of the Skin*, Philadelphia, P. Blakiston's Son & Co., p. 473.

8. Sutton: *Diseases of the Skin*, St. Louis, The C. V. Mosby Co., p. 170.

9. Allbutt and Rolleston: *System of Medicine*, New York, Macmillan Co., **9**:348.

10. Schamberg: *Diseases of the Skin and the Eruptive Fevers*, Philadelphia, W. B. Saunders Company, p. 115.

11. Whitfield: *Skin Diseases and Their Treatment*, New York, Longmans, Greene & Co., p. 199.

schild" eyebrow sign ¹²); yellowish, straight, long teeth which were carious and showed extensive pyorrhea; thyroid gland not palpable; relaxation of ligaments (dorsal kyphosis and lumbar lordosis); poor muscular tone (pot-belly); extreme constipation relieved while under treatment; slow pulse; chilliness and a tendency to contract "colds"; a dry, scaly, itchy skin; and finally, the local and systemic benefits derived from the thyroid administration.

Disorders of the thyroid gland are productive of changes in the structure and functions of almost all the tissues and organs of the body. The symptoms which develop may result in well recognized clinical entities like cretinism, myxedema and exophthalmic goiter, or, on the other hand, they may be of such a minor or indefinite nature that their relation to thyroid dyscrasia may not be considered unless one bears in mind the possibility of disturbed endocrine function. The administration of thyroid is therefore justifiable in cases showing minor symptoms of hypothyroidism, and improvement under such therapy should afford a valuable therapeutic test. Even in those cases in which thyroid symptoms are not present, organotherapy should be tried as it has been noted that the effects of thyroid extract on the skin are improved nutrition, increased glandular activity and excretion of waste products, stimulation of hair growths and enhancement in desquamation of an unhealthy, horny skin layer with the reproduction of a new covering. These effects are particularly to be desired in all the general hyperkeratotic conditions like ichthyosis and pityriasis rubra pilaris, which are associated with faulty metabolism.

SUMMARY AND CONCLUSIONS

A report is made of a typical case of pityriasis rubra pilaris occurring in a male adult who revealed more or less definite signs and symptoms of thyroid dysfunction. The skin condition showed rapid improvement and an apparent cure was obtained with thyroid therapy alone. No claim is advanced for the specificity of thyroid extract in the cure of this disease, but it is recommended that organotherapy should be given a trial in the treatment of pityriasis rubra pilaris, and only by further study and careful clinical observations will its actual therapeutic value and effects be definitely determined.

12. Cobb: *Organs of Internal Secretions*, New York, William Wood & Co., p. 65.

NOTES FROM KALAHI LEPROSY HOSPITAL

JAMES T. WAYSON, M.D.

Medical Superintendent

HONOLULU, H. I.

The Kalihi Leprosy Hospital is owned, equipped and conducted by the Territorial Board of Health. It is located three miles from town and comprises five or six acres. The buildings include several dormitories, an infirmary, dispensaries, examination rooms, kitchen, dining rooms, assembly hall and steam laundry, all equipped with hot and cold water and electric lights and a school for children. There are in addition recreation grounds, tennis and volley ball courts, billiard rooms, vegetable gardens, piggery, poultry runs, etc. Adjoining the hospital grounds are the laboratories, library and other buildings of the United States Public Health Service Leprosy Investigation Station, directed by Dr. J. T. McDonald, who is also ex-officio attending physician to the hospital.

On July 10, 1920, there were 117 patients, the majority of whom were Hawaiians—sixty-four females and fifty three males; the oldest patient was 62 years, the youngest 7 years, and the average age was 23 years. It should be stated that as a rule males predominate. On this date none of the patients was bedridden, and they were otherwise in good health. The prevailing spirit is one of hope and cheerfulness, and the morale is excellent. Most of the cases are early types, many of the patients having entered the hospital voluntarily. As a rule the patients remain in the Kalihi Hospital six months, or, if they show marked improvement, for longer periods. At the end of their stay they are either paroled or sent to the Molokai Settlement 50 miles away.

The standard treatment here now is the use of ethyl esters of the fatty acids made from the whole crude chaulmoogra oil in the laboratories of the College of Hawaii, according to methods devised by the president, D. A. L. Dean. This preparation carries 2 per cent. of iodine by weight in chemical combination. The preparation is injected intramuscularly into the gluteal region, the initial dose being 1 c.c. per week, later doses being gradually increased to 5 c.c. or 6 c.c. weekly. The preparation contains all the therapeutic virtues of the crude oil, and is almost as fluid and limpid as water, being entirely absorbed in 24 to 48 hours. Internally, appropriate doses of the mixed fatty acids, carrying 2.5 per cent. iodine in chemical combination, are given in capsules three times a day. The preparation is partly predigested in the

laboratory and rarely causes nausea. In addition to treatment with the above mentioned preparations or modifications of chaulmoogra oil, numerous accessory treatments are used, such as strychnin, iron tonics, arsenous acid, hot baths, liniments, escharotics, unguents, heliotherapy and other treatments.

The results have been encouraging. In the period from Dec. 24, 1918, to July 10, 1920, seventy-eight patients have been paroled from segregation and there has not been a single recurrence.

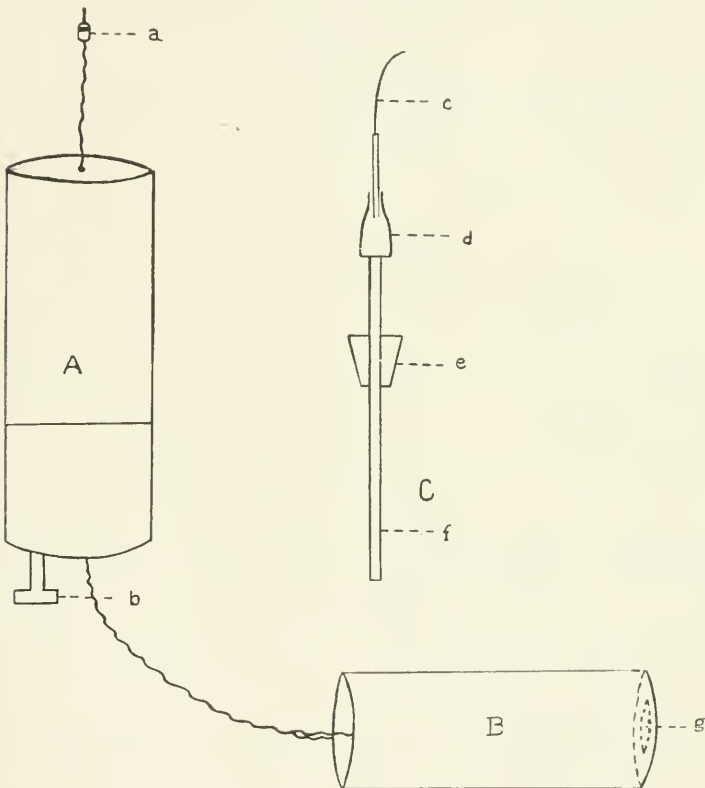
Among the hospital patients, over 10 per cent. have one or more attacks of leprosy fever with macular eruption, but they soon recover from these acute attacks and are in better condition than they were before.

REMOVAL OF WARTS

THEODORE K. LAWLESS, M.S., M.D.

CHICAGO

The multiform warts or verruca usually filiform in type, which occur most frequently on the face, especially on the bearded region, and on the hands, present some difficulties in treatment. First, they are auto-inoculable, and tend to spread very rapidly; second, they are multiform; and third, those on the face require some special care in order not to cause too much scarring with its resultant disfigurement.



A, transformer; a, socket and plug; b, current regulator. B, resonator and insulated needle holder; g, receiver for needle holder. C, electrode and needle attachment; c, platinum needle; d, grip; e, cork stay to fit snugly at g; f, pole.

After a careful and thorough trial, I offer the method for treatment here described, which has, in careful hands, these advantages: It is practically painless; only the most superficial scarring remains; there are no recurrences at the site of previous lesions; and it is very rapid in producing results.

The ordinary high frequency apparatus is used with the exception of the glass vacuum tube, instead of which, a metallic needle holder is used of such length that when it is inserted into the chamber of the high frequency apparatus an electric contact is formed. In the needle holder, a fine platinum or a very fine sewing machine needle is inserted and made secure.

One of the two methods may be employed after injecting a small amount of procain into the bases of the lesions: The needle may first be slipped into the base of the wart and the current turned on gently, then the current is gradually intensified until a small blister forms at the base of the wart: or the needle may be held and gently pressed at the apex of the lesion or brought within one-fourth to one-eighth of an inch of the lesion and sparked in either of the two last positions until moderate charring is observed at the apex, and the lesion becomes whitish. Experience alone is the best guide as to the strength of current, and the time of exposure in order to produce the least amount of scarring.

CONCLUSIONS

1. The method is practically painless.
2. It is safer than the roentgen ray.
3. It is bloodless.
4. There is less scarring than when curettage, followed by strong caustics, is employed.
5. No recurrences occur at the site of previous lesions.
6. Rapid results are produced.
7. It may be used with or without local anesthesia, but it is slightly uncomfortable without its use.

A STUDY OF A CASE OF YAWS (FRAMBESIA
TROPICA) CONTRACTED BY AN AMER-
ICAN SOLDIER IN FRANCE *

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Yaws, or frambesia, is essentially a tropical infectious and contagious disease caused by *Spirochaeta pertenuis* and characterized by a frambesiform granulomatous eruption.

Our knowledge of yaws is due to the following investigators: Char-
louis,¹ who in 1881 proved by actual experiment that syphilis and yaws
are two distinct maladies. This investigator inoculated thirty-two
Chinese prisoners with crusts and scrapings from yaws lesions, and in
twenty-eight instances succeeded in producing characteristic yaws. He
also succeeded in inoculating a native suffering from yaws with syphilis,
thereby definitely disproving the assumption that the two conditions
were one and the same. It is a further matter of established fact that
a syphilitic patient may contract yaws in the usual manner, as well as
experimentally. For our clinical knowledge of yaws, we owe much
to Numa Rat² and more recently to Castellani.³ Rat's report, pub-
lished in 1891, has become classic. The most important contribution
to the history of the disease was the discovery of the causative agent
(*Spirochaeta pertenuis*) by Aldo Castellani³ in 1905. The organism
was cultivated in 1912 by Noguchi,⁴ and important immunologic studies
have since been made, notably by Neisser,⁵ Nichols⁶ and others.

Few, if any, genuine cases of yaws have been reported in which the
disease was contracted in regions other than the countries in which it is
endemic. However, cases of imported yaws occurring in nontropical

* A contribution from the Dermatological Research Institute, Philadelphia.

* Read at the Forty-Third Annual Meeting of the American Dermatological
Association, Asheville, N. C., April, 1920.

1. Vierteljahrschr. f. Dermatol. u. Syph. 8: 1881.

2. Rat, N.: Framboesia (Yaws): Its Nature and Treatment, London, 1891.

3. Castellani: J. Ceylon Branch Brit. Med. Assn., 6:17, 1905.

4. Noguchi: München. med. Wchnschr. 58:1550, 1911.

5. Neisser, Baermann and Halberstädter: München. med. Wchnschr. 53:
1337, 1906.

6. Nichols: J. Exper. Med. 12:616, 1910; 14:196, 1911.

countries have been reported in the literature. French writers (Breton, Rocheford and Labat) state that yaws occurred along the Mississippi river among the Indians, especially among the tribe of Caribs. Wood⁷ reviews all the cases of yaws reported in the United States from the first authentic reference of the disease by Buckell, in 1737, to the year 1915. There were nine cases in all, including the case reported by Wood. Some of these were imported from tropical countries. In other cases the genuineness of the diagnosis may be questioned, particularly in view of the absence of laboratory evidence. In the case reported by White and Tyzzer⁸ the disease was observed in a West Indian. This case was probably an imported one.

In the case reported by us the disease was contracted in France, probably through contact with an infected man stationed there during the war.

In a personal communication to us concerning this case, Castellani writes:

From the description you give and the photographs, I would diagnose the case as one of yaws. I am not aware of the disease being previously recorded in France, but of course during the war a large number of native troops and workmen were imported into France from the tropical countries, and they may have imported the disease with them. As regards mode of infection, I am inclined to give more importance to direct contact than to insect carriers. Of course, in the tropics there is no doubt that in many cases the disease is carried by flies.

Dr. John A. Fordyce⁹ has personally communicated to us information concerning an American sailor who contracted yaws while on duty at Brest, France.

Cassar¹⁰ reports an observation on a patient with a tertiary case of yaws whom he had seen in France, September, 1918. This patient, an Annamite, was a soldier in the French army, who contracted yaws some years before in Ho-Keou. This is the only report of yaws occurring among soldiers recently mobilized in France that we have been able to find in the literature.

REPORT OF A CASE

The following is the history of an American soldier, in whom a clinical diagnosis of yaws was made. He contracted the disease while serving in France. He was admitted to the dermatologic service of Dr. Jay Frank Schamberg, at the Philadelphia General Hospital, Dec. 30, 1919.

7. Wood: *Am. J. Trop. Dis.* **2**:431, 1915.

8. White and Tyzzer: *Jour. Cutan Dis.* **29**:138, 1911.

9. Since this paper was written, C. S. Stephenson [*Military Surgeon* **47**:344 (Sept.) 1920] reports a case of yaws occurring in an American sailor who was infected in Brest, France. This case, we believe, is the same one mentioned above in a personal communication from Dr. John A. Fordyce.

10. Cassar: *Ann. de dermat. et syph.* **7**:12, 1919.

The family history had no bearing on the condition. The patient was born in Philadelphia. He denied having had any infectious disease, gonorrhea or syphilis. His occupation prior to army service was that of a plumber's helper.

He joined the Royal Canadian Army, enlisting in Canada, during the early part of 1917, and was sent to England a few months later. He arrived at Folkstone and remained there for three weeks; he was then sent to France. At this time he was a member of the Royal Canadian Dragoons (cavalry), and he remained with this branch of the service until he was discharged in 1919. The members of this organization were composed of Americans and Canadians. He arrived in France about July, 1917, departing about August,



Fig. 1.—Circumscribed, infiltrated raised patches on scalp.

1919; most of this time, at intervals of fifteen months, was spent at Etappes in the northern part of France. This place was a large base for cavalry and infantry troops. Thousands of soldiers were gathered here: Canadians, Australians, New Zealanders, South Africans (white men), New Foundlanders and Chinese—labor battalion. He said that there were no soldiers from Algeria or India, indeed no other men than white, except negroes from Canada and Australia. About the longest time that he was away from Etappes was for three months, which were spent at Cambrai and its environment. On this occasion the cavalry followed in the wake of the tank attack on the German lines. For a time he was stationed at Valency and Mont-Gardens. The only time he saw dark skinned soldiers of the Allies was when he would meet them along the streets or in such places as saloons and Y. M. C. A. huts. At no time was he in close contact with them, such as sleeping in the same barracks.

He left France during the early part of August, 1919, from the port of Boulogne. Prior to this time he was stationed at the base at Etappes for some months. On the boat crossing the channel there were only Canadian troops. He arrived at Folkstone, England, and then went directly to Aldershot, England, to the Duke of Connaught Hospital. He was sent to the hospital from France on account of illness. The first symptoms noticed (while at Etappes) were rheumatoid pains in the knees and shoulders. At times these pains were sufficiently severe to incapacitate him. He had no other complaint. He traveled from France to the hospital in England as an ambulatory case. On arrival at the hospital he was confined to bed; later he had fever, 104 to 105 F., for three or four days. He was in the hospital one month, the pain gradually disappearing; he had no skin manifestation at this time. In the

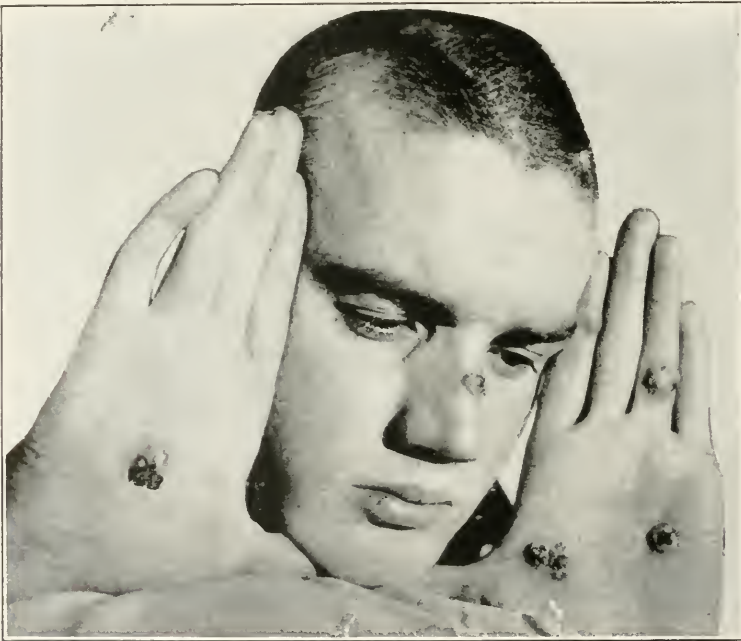


Fig. 2.—Lesions on nose and hands.

same hospital and in the same ward were British troops recently returned from India, suffering from malaria. He also came in contact with a white man from Africa, who, in the patient's opinion, had similar lesions to those the patient had when he came under our observation.

He left the hospital about the middle of September, en route to Whitly, England, awaiting debarkation. He remained there for one week and was then sent to Liverpool; he sailed from that port and landed at Halifax in the early part of October. He was sent to Toronto for discharge on October 15. From Toronto he came directly to his home in Philadelphia. He was feeling well at that time. About a week after his return he first noticed small "pimples" on his palms which gradually became larger until they reached the size of the present lesions. One week later lesions appeared on the scalp and soles of his feet, although he felt well.

Physical Examination.—The general physical examination was negative except for a generalized adenopathy. The lymph nodes, with the exception of the epitrochlears, were about the size of almonds.

Dermatologic Examination.—The eruption was distributed on the palms, soles, scalp, forearms, throat and penis.

On the scalp there were five distinct areas of circumscribed, infiltrated raised patches, exhibiting a distinct elevated border and central depression and covered with a firm, bright yellow crust. The patches in the main were roundish, except where the lesions had coalesced. They were approximately of the size of a five-cent piece. On the left side of the scalp, in the parieto-occipital



Fig. 3.—Lesions on palms of hands.

region, was a coalescent patch 8 by 4 cm. One of the patches was of crescentic shape with a raised border and a cicatricial base and center, where ulceration had previously been present (Fig. 1).

The lesions in general had a verrucoid and papillomatous surface and bore a general resemblance to the lesions of blastomycosis. For the greater part, the patches appeared to be devoid of hair. On the center of the dorsum of the nose, there was a conical, rounded lesion about 1 cm. in diameter, projecting about 5 mm. above the level of the skin and covered with a yellow and brown crust. The other lesions were situated as follows: a lesion the size of a five-cent piece on the posterior aspect of the arm, near the elbow; one, half that size on the flexor surface of the arm nearby (Fig. 2); one large lesion on the palm of each hand (Fig. 3); one lesion 1.5 cm. in diameter on the flexor aspect of the third phalanx of the ring finger of the left hand; three well developed lesions on the plantar surface of the right foot. There

was one lesion on the interdigital space (between the great and first toe). A lesion, the size of a quarter, was on the outer aspect of the right foot below the malleolus (Fig. 4). There were two large lesions, oval in shape and varying in a general way in size from that of one cent to that of a five-cent piece, on the inner side of the left leg, just above the malleolus. Another lesion the size of a five-cent piece was situated in the popliteal space. Nearly all of the latter lesions were elevated 5 mm. or so above the skin and had a distinct fungoid or papillomatous appearance. Many were covered with a crust, which on being detached, through violence, exposed an irregular, reddish, ulcerated surface. The palmar and plantar lesions projected well above the skin level, and showed an irregular, wartlike surface, covered with reddish and yellowish crusts. On the left forefinger, and scattered elsewhere on the palmar aspects of the fingers, were pinhead sized and large sized conical, papular reddish spots, with central horny plugs. As the central plugs fell out they left a depressed central pit.¹¹

On the prepuce were numerous wartlike excrescences which bore a rough resemblance to condylomata acuminata.

On the columna of the nose and on the left nostril were two, lentil-sized to pea-sized, obtuse, dull red elevations.

Stretching across the entire soft palate was a band, about 2 cm. in diameter, of a filmy whitish discoloration on a slightly inflammatory base. It had an appearance intermediate in character between a huge mucous patch and a leukoplakia. There was also a whitish noninflammatory patch on the right buccal membrane.

Dark Field Examination.—The serum obtained from the surface of some of the skin lesions showed spirochetes having the morphologic characteristics of *Spirochæta pallida*. The secretion obtained from the throat lesion was negative.

Wassermann Reaction.—The Wassermann reaction was + + + + with cholesterolized, alcoholic, syphilitic liver and acetone, insoluble lipoid antigens.

Blood culture was negative. Intratesticular injection into rabbits was made with an emulsion from one of the skin lesions. The results are given under the head "Experimental Studies."

Histopathology.—The microscopic changes in the skin in yaws have been carefully studied by Unna, MacLeod, Jeanselme, Plehn, and in more recent years, by Schüffner, Marshall, Shennan, Siebert, Ashburn, Craig, Löhe, and White.

Briefly stated, the changes found are: a marked thickening in the epidermis with elongation of the rete pegs; swelling, vacuolation and degeneration of the epithelial cells; not infrequently sharply circumscribed areas in the epidermis containing polymorphonuclear leukocytes and detritus (these in reality represent miliary abscesses, in which spirochetes are not infrequently found); marked edema of the corium and the presence of a diffuse cellular infiltration made of polymorphonuclear leukocytes, large and small mononuclear leukocytes, eosinophils, plasma and mast cells and connective tissue cells. In nodules that have existed for some time plasma cells are seen in large numbers.

11. These lesions bear some resemblance to "follicles." Castellani described lesions of a similar nature and referred to them as a "peculiar frambeside of the palms"; Castellani and Chalmers: *Manual of Tropical Diseases*, Ed. 3, p. 1550.

MacLeod has called attention to the fact that there is no perivascular cell infiltration nor endothelial proliferation, and that this contrast is of great importance in the differentiation from syphilis. In yaws, there are more changes in the epidermis and less in the corium than in syphilis. Furthermore, greater edema in the corium is encountered, and giant cells are as a rule absent.

In our own case, a nodule was removed from the right forearm and stained for histologic study; it was also stained with the Levaditi stain for spirochetes.

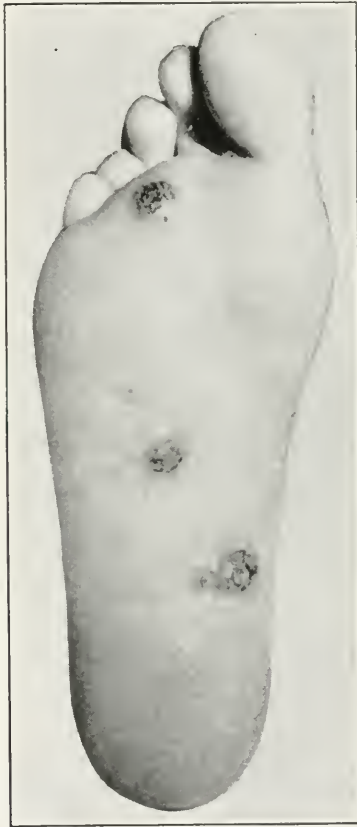


Fig. 4.—Lesions on right foot.

A well pronounced necrotic crust (Fig. 5) was seen covering a part of the epidermal surface. There was enormous hyperplasia of the epiderm, with great thickening and elongation of the papillary rete projections (Figs. 6 and 7). Parts of the epidermis appeared to be changed, but elsewhere the intercellular spaces were infiltrated with polymorphonuclear leukocytes. In one area a distinct miliary abscess was seen on a level with the summits of the papillae; in this abscess seven or eight spirochetes were seen in the Levaditi stained sections (Fig. 8).

Some of the epithelial cells exhibited a degenerative change. Throughout the corium edema was present, and a rich polymorphonuclear leukocyte infil-

tration was seen. Lymphocytes and plasma cells were present in moderate numbers.

The blood vessels exhibited no perivascular change, an observation corroborated by Prof. Allen J. Smith of the University of Pennsylvania and Prof. Randle C. Rosenberger of the Jefferson Medical College.

Treatment.—Neo-arsphenamin, 0.9 gm., was administered intravenously, resulting in the disappearance of many of the lesions and marked improvement in others in a fortnight. Fourteen days later a second injection of the same dose was given, which caused a complete resolution of the remaining lesions (Fig. 9). The Wassermann reaction at this time, performed with the three stated antigens, was + + + +. Frequent Wassermann tests were performed, and the reaction remained + + + + until the end of February, 1920, at which time the reaction was + + + with the syphilitic liver antigen, but remained at + + + + with the other two antigens. The table is a chronologic record of treatment and of the Wassermann reactions.

WASSERMANN REACTION

Date	Antigens		
	Cholesterolized	Alcoholic Syphilitic Liver	Acetone Insoluble Lipoids
Jan. 2, 1920.....	+ + + +	+ + + +	+ + + +
Jan. 9, 1920.....	+ + + +	+ + + +	+ + + +
Jan. 16, 1920.....	+ + + +	+ + + +	+ + + +
Jan. 22, 1920*.....	+ + + +	+ + + +	+ + + +
Feb. 1, 1920.....	+ + + +	+ + + +	+ + + +
Feb. 5, 1920*.....	Test not performed		
Feb. 13, 1920.....	+ + + +	+ + + +	+ + + +
Feb. 22, 1920.....	+ + + +	+ + + +	+ + + +
Feb. 26, 1920.....	+ + + +	+ + + +	+ + + +
March 4, 1920.....	+ + + +	+ + + +	+ + + +
March 19, 1920.....	+ + + +	+ +	+ +
April 2, 1920.....	+ + + +	+ +	+ +
April 9, 1920.....	+ + + +	+ +	+ +
April 14, 1920*.....	Test not performed		
April 19, 1920.....	+ + +	+ +	+ +
July 8, 1920.....	—	Neu.	Neu.

* 0.9 gm. neo-arsphenamin given intravenously.

A third intravenous injection of 0.9 gm. of neo-arsphenamin was given in April, 1920. No further Wassermann tests were made until July, 1920, at which time the tests showed a + reaction with the cholesterolized antigen and a negative reaction with the alcoholic liver and acetone insoluble lipid antigens. The patient has remained subjectively well and has been free of any clinical occurrence.

PARASITOLOGY

Yaws, like syphilis, is a spirochetel disease. To the student of syphilis it is of particular interest since it is in many ways similar to this disease clinically and biologically. So closely clinically do the two diseases simulate each other that differential diagnosis is often difficult; indeed for a long time it was maintained by many that yaws was a tropical form of syphilis. No less an authority than Jonathan

Hutchinson concurred in this opinion. As we shall point out, the laboratory differentiation of the two diseases is likewise difficult. A knowledge of yaws is perhaps of aid to a better understanding of the immunologic problems of spirochetal diseases. A summarization of our knowledge of the differences in immunity tests, experimental lesions and in serum reactions between the two organisms is of interest.

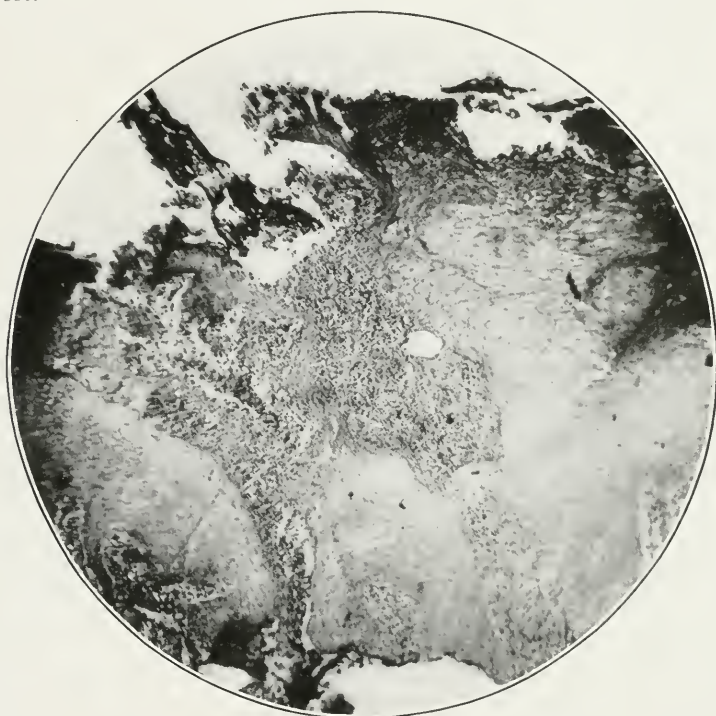


Fig. 5.—Section of yaw stained with hematoxylin and eosin; necrotic crust overlies a part of the epidermal surface of the lesion with dense infiltration with polymorphonuclear leukocytes; $\times 70$.

Spirochaeta pertenuis is an extremely delicate spiral-shaped organism, varying in length from a few microns to 18 to 20 microns and even more. The organism belongs to the genus *Spirochaeta* (Schaudinn, 1905), the type organism of which is the *Spirochaeta pallida* (Schaudinn and Hoffman, 1905). The measurements of this genus, according to Noguchi are:

Length: 16 to 14 microns; pointed ends. Diameter: 0.25 to 0.3 microns, cylindrical. Spiral amplitude: 1 micron; regular, rigid; spiral depth: 0.8 to 1 micron; very constant. Waves: one or more slight undulating curves may be present. Axial filament: doubtful. The whole seems to consist of a spirally wound axial filament. Chambered structure: absent. Membrane: doubtful; if

there is one it must be flexible. Crista: absent. Terminal finely spiral filament: present; easily seen in cultures. Flagella: absent; highly motile end portion: absent. Division: transverse or possibly also longitudinal. Habitat of genus: two pathogenic and several harmless parasites. Other species: *pertenuis*, *microdentium*, *macrodentium*, *mucosum*, *calligyrum*, *minutum*. Staining properties of axial filament and cell membrane: membrane not recognizable.

Schaudinn and Castellani considered *Spirochaeta pallida* and *Spirochaeta pertenuis* practically morphologically identical, although Blanchard, Morton, Prowazek, Russell and others have pointed out some slight morphologic differences. This morphologic similarity exists among the entire species of the genus *Spirochaeta*, but notably among *Spirochaeta pallida*, *S. pertenuis* *mucosum* and *microdentium*. It is the consensus of opinion that the two organisms are morphologically indistinguishable. In this regard Castellani¹² states: "We believe that the differentiation of the two organisms . . . is to be based more on the biological results than on slight morphological differences."

We have observed *Spirochaeta pertenuis* in the dark field microscope with one portion of the organism straight and the remaining portion with the characteristic coils preserved. This has been observed only when the organism was in contact with obstacles. Castellani has also observed this phenomenon. The above morphologic changes can be contrasted with a similar change occurring in two organisms, *Leptospira icterohaemorrhagiae* (Inada and Ido) and *Leptospira icteroides* (Noguchi). The former is the causative agent of infectious jaundice and the latter of yellow fever. This change, as described by Noguchi, is as follows: *Leptospira icterohaemorrhagiae*, in the dark field picture in free space, is seen as a rapidly motile organism with a number of fine spirals with one or both ends semicircularly hooked. When motion ceases, many of them lose the typical hooks; when penetrating semifluid mediums, the organisms become serpentine, waved, and assume large wavy undulations, and the typical hooked ends disappear. When penetrating semisolid mediums, the organism again assumes a change in morphology. The change in the morphology of *Leptospira icteroides*, as given by Noguchi,¹³ is somewhat similar to *Leptospira icterohaemorrhagiae*.

As we shall later point out, the morphologic deviation is more apparent in stained specimens of the organism. We have never observed a similar change in the morphology of the *Spirochaeta pallida* either in dark field or in stained specimens from human lesions.¹⁴ In speci-

12. Castellani: J. Trop. Med. **9**:3, 1916.

13. Noguchi: J. Exper. Med. **30**:1, 1919.

14. However, we find a reference by Noguchi in his Harvey lecture on "Spirochaetes," in which he states that organisms obtained from syphilomas of rabbits' testicles, immediately fixed and stained, exhibit striking irregularity of curves unlike the accustomed picture.

mens from human sources, the coils remain constant. Schaudinn states that under unusual conditions the coils are obliterated, and straight and artificial forms are seen. It is well known, and has been observed by us, that culture specimens of *pallidum* exhibit morphologic variations. Under such circumstances, irregular forms may be seen, the organism tending to become short and plump.

Staining Properties of Spirochaeta Pertenuis.—It is generally stated by writers that *Spirochaeta pertenuis* stains with difficulty. This has been our experience, and there is no doubt that this organism is more

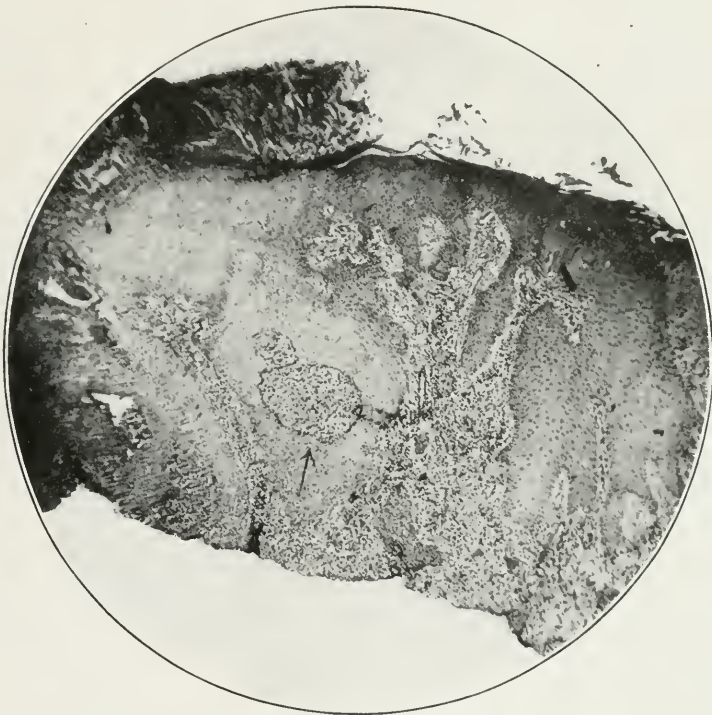


Fig. 6.—Section of yaw stained with hematoxylin and eosin showing epidermal changes. The arrow points to a circumscribed collection of polymorphonuclear leukocytes in the epidermis; $\times 70$.

difficult to stain than *Spirochaeta pallida*.¹⁵ For staining the organism Castellani recommends Leishman's stain, the alcoholic solution to act for five minutes, and the subsequent admixture with distilled water

15. Indeed, in our opinion, the lesser affinity of *S. pertenuis* for the usual spirochetal stains is so striking as to constitute a point of important differential value. We have never had much difficulty in staining the *S. pallida*, but we have experienced the greatest difficulty in obtaining satisfactory stained specimens from our case of yaws, although scores of slides were stained.

for from one half hour to several hours. Other writers recommend one of the Romanowsky stains (Giemsa, Wright, Leishman), pointing out that it is necessary to have the stain act for from a few hours to many hours. With these stains we were unable to obtain satisfactory results; the organism was either faintly stained or not stained at all. With the Fontana stain we succeeded in staining what we considered to be the organism but with curves entirely obliterated. We obtained the best results with the anilin black stain of Rosenberger and Fanz. With this stain many of the organisms were well stained, but the organism did not appear so regularly curled as is shown in the dark field picture. Again, and this point we wish to emphasize, some appeared with one portion entirely straight and the remaining portion either with the curves intact or the curves were much more irregular and coarse (Figs. 10 and 11). Thus it was apparent to us that the stained organism presented a changed morphology. The curves in stained specimens of *Spirochaeta pallida* are perhaps less regular than in the dark field picture, but this change is considerably less apparent than with *Spirochaeta pertenuis* (Fig. 12). The truth of this becomes apparent when one contrasts published photomicrographic pictures of the pallidum and pertenuis. In this regard we may quote Bosanquet's¹⁶ statement: "In the illustrations given by Castellani, *Spirochaeta pertenuis* does not appear so regularly curled as is *Spirochaeta pallida*." In Ashburn and Craig's¹⁷ study of the *Spirochaeta pertenuis* they observed many variations in the shape of the stained organism, which they describe by dividing them into seventeen different types or classes. In the diagrammatic illustration of the types of stained specimens, these morphologic changes are well shown. They attributed the changed morphology to physical forces acting on the organism during the making and drying of stained specimens. They contrasted this change with similar changes that a spiral wire spring could be made to present when subjected to analogous forces when one or more of its coils are straightened out by traction and pressure. This explanation is doubtless correct; however, since all spiral organisms when stained do not present such marked morphologic changes, it must be regarded as a characteristic of *Spirochaeta pertenuis* and is valuable in the differentiation of stained specimens of *S. pallida* and *S. pertenuis*.

Leptospira icterohaemorrhagiae and *Leptospira icteroides* when stained may appear different than in the dark field. Noguchi¹⁸ has shown that the natural features of these organisms can be well pre-

16. Bosanquet: Spirochetes, Philadelphia, W. B. Saunders Company, 1911.

17. Ashburn and Craig: Philippine J. Sc. **2**:441, 1907.

18. Noguchi: J. Exper. Med. **25**:755, 1917; **27**:575, 1918; **30**:1, 1919.

served when they are fixed in osmic acid vapor and then stained over night with Giemsa's solution. Noguchi states that specimens of *Leptospira icteroides* fixed with methyl alcohol seldom retain the elementary spirals, and that the beauty of the organism as it appears by dark field illumination is never well retained in a stained preparation, even in the best specimens. In the latter, it appears almost as a totally different organism. This is apparently true also of *S. pertenuis*. For staining this organism Schüffner¹⁹ states that most satis-

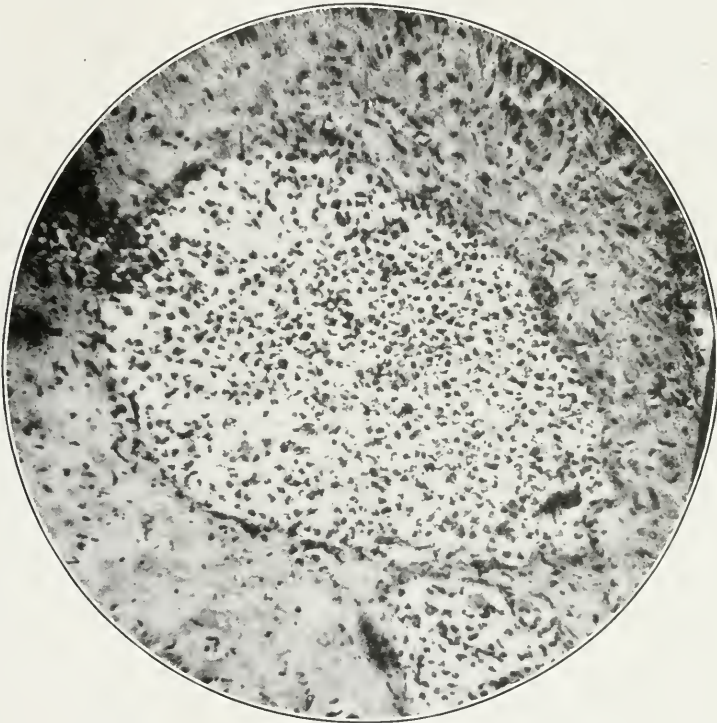


Fig. 7.—Circumscribed islet of polymorphonuclear leukocytes in the epidermis indicated by the arrow in Figure 6; $\times 288$.

factory results are obtained by Romanowsky stain when preceded by osmic acid or formaldehyd vapor fixation. Further endeavors to obtain better stained specimens of *S. pertenuis* are being made by us.

Distribution of Spirochaeta Pertenuis in Tissues.—The organism is constantly found in the primary and secondary lesions, but rarely in the tertiary lesions. In men, they have been demonstrated in the splenic blood and in the blood of the general circulation and in the bone marrow of inoculated animals. They have never been found in

19. Schüffner: München. med. Wchnschr. **44**:1364, 1907.

the cerebrospinal fluid, nor has their presence been demonstrated in this fluid by animal inoculation. This observation is consistent with our clinical knowledge concerning the absence of neurol involvement.

Although there is a generalization of the parasite in yaws, pathologic visceral changes have not been demonstrated in man, and tertiary manifestations are relatively rare.

EXPERIMENTAL LESIONS IN THE RABBIT AND MONKEY

The susceptibility of the rabbit's testicle to syphilitic infection is duplicated with *Spirochaeta pertenuis*. Indeed, this susceptibility is successful in a greater percentage of cases than with *S. pallida*.

The species of animal used and the source of the virus and its concentration are factors that influence the percentage of positive inoculations with each organism.

Up to the present writing, six months since the initial inoculation of rabbits' testicles with a yaws lesion from the case herein reported, we have carried this strain of *S. pertenuis* through four transfers in rabbits.²⁰

Technic of Testicular Inoculation.—A yaws nodule removed from the patient's forearm was placed in a sterile mortar and finely minced with scissors. Sufficient sterile salt solution (0.85 per cent.) was added to make an emulsion containing from one to three spirochetes to the microscopic field. The fluid emulsion was aspirated into a small glass syringe fitted with a 20 gage needle, about three-quarters inch in length. The scrotum of the animal to be inoculated was painted with dilute tincture of iodine, and 0.5 c.c. to 1 c.c., depending on the size of the testicle, was injected into the center of each organ.

Rabbit transfers were made by removing aseptically an infected testicle. An infected node was removed and made into an emulsion as above described. Other rabbits were inoculated with this emulsion, the strength of which was approximately the same for each transfer.

Technic of Scrotal Inoculation.—The scrotum of the animal to be inoculated was painted with dilute tincture of iodine. A 16 gage needle was inserted just beneath the skin of the scrotum. A portion of a node from an infected rabbit's testicle was inserted through this needle by means of a wide trocar. In some animals the infected tissue was placed in the tunica vaginalis.

Technic of Inoculation of Anterior Chamber of the Eye.—The eye of the animal to be inoculated was cocainized with a 2 per cent. solution, an eye speculum was inserted and the eye fixed with a forceps. The anterior chamber was punctured with a 23 gage platinum needle inserted at the sclerocorneal junction. This procedure resulted in the evacuation of aqueous fluid and the collapse of the anterior chamber. To the needle was fitted a Fournier syringe, and three or four minims of an infected emulsion was injected.

Technic of Intravenous Injection.—Five c.c. of blood were withdrawn by venipuncture from the yaws patient. At the time of this withdrawal the

20. The organism is still under observation in rabbits and further studies are being conducted.

patient had not been treated and was in the acute stage of yaws. To this blood were added 5 c.c. of a 1 per cent. solution of sodium citrate in normal salt. This mixture was injected into the vein of the ear of each rabbit.

Technic of Inoculation of a Monkey.—On the eyebrow of a monkey a scarification was made, and on this area was rubbed a portion of a yaws lesion removed from the patient. A dark field examination of this yaws lesion disclosed many actively motile spirochetes. Another and similar attempt to inoculate a monkey's eyebrow was made with a node removed from an infected rabbit's testicle. In addition, an emulsion made from this node was injected subcutaneously in the region of the eyebrow.

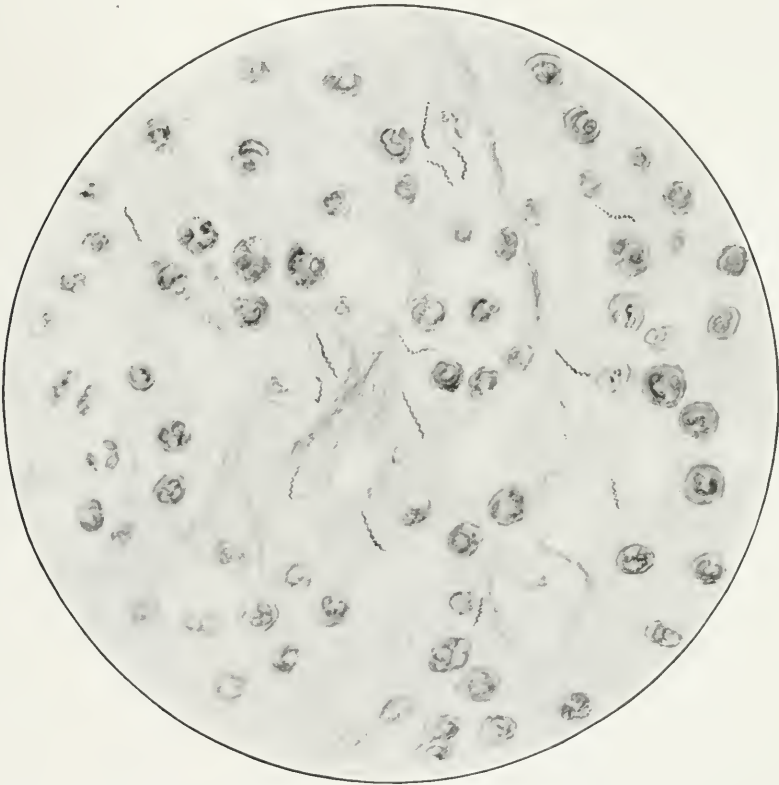


Fig. 8.—Islet of polymorphonuclear leukocytes in the epidermis indicated by the arrow in Figure 6. This section was stained by the Levaditi method to show *S. pertenuis*; $\times 700$.

Testicular Lesions in the Rabbit.—We succeeded only in obtaining one variety of yaws lesion in the rabbit, namely, testicular. We failed to produce corneal and scrotal lesions and to infect the rabbit intravenously by the injection of the blood of the yaws patient while in the acute stage of the disease.

In the first series of rabbit inoculations, there were 50 per cent. positive results with an incubation period of about thirty-four days. In this series some died before the expiration of thirty-four days, and one was killed because of the development of a contagious infection. In the second transfer 75 per cent. gave a positive result with an incubation period of about thirty-nine days. In the fourth transfer 37 per cent. gave a positive result with an incubation period of about sixty-five days.²¹ In Nichols' ²² series, the incubation period with inoculation of fluid of lesions of the testicles, caused by *Spirochaeta pertenuis*, was forty-five days for the animal in the first transfer; for the last animals in the ninth to the fourth transfers it was twenty-nine days. With tissue inoculation the period averaged from twenty-three to twenty-five days. For the entire series of fifty-two animals, the incubation period was twenty-six days, or eight days shorter than the period required by his series of rabbits inoculated with *Spirochaeta pallida*.

There are essentially no differences in the experimental testicular lesions of syphilis and of yaws. From our examination of a testicle infected with yaws, this is apparently the case histologically. This examination disclosed similar changes to those resulting from syphilitic infection.

In the majority of our positive rabbits the inoculation first became apparent in an enlargement of the scrotum. This enlargement consisted of edema, and on puncturing the tunica vaginalis a gelatinous fluid was obtained, which contained *Spirochaeta pertenuis*. The appearance of edema usually forecast the development of one or several nodes, either in the epididymis, in the testicle or in both organs. The nodes (lesions), at first just appreciable to touch, developed to about the size of a pea. We did not observe lesions much larger than a pea; occasionally they did not progress to the size of a pea and these lesions rapidly disappeared. On puncturing the lesions numerous spirochetes were found. The organism was almost twice the length of the same organism studied from the original yaws lesion in the patient, and they were further characterized by the change of morphology already described. After removing the infected testicle, grossly the lesion was sharply margined and cartilaginous in consistency. Figure 13 is a photograph of the positive rabbits. The scrotum is enlarged and edematous. In each testicle a node was palpable.

In the infected lesions, numerous and freely motile *Spirochaetae pertenuis* could be demonstrated for only a short period, about ten days. After this period the organisms would suddenly disappear in

21. About ten rabbits were used in each transfer.

22. Nichols: J. Exper. Med. **14**:199, 1911.

the aspirated fluid. However, after a variable period they were again present in large numbers. In the interval between their disappearance and reappearance the gross appearance of the infected organ would remain unchanged and the infected nodules were palpably the same; no organism, either motile or nonmotile, could be demonstrated on puncture. At the time of reappearance of the organisms, the infected testicle was edematous. Our transfers were always made at the time the punctures showed numerous and freely motile organisms. How-



Fig. 9.—Disappearance of lesions after treatment.

ever, we made one transfer, during the time the organisms could not be demonstrated, by puncturing an infected node. The dark field examination of this infected node after removal was negative, yet, curiously the transfer made from this node gave a positive result with an incubation period of eighteen days. Further studies are being made concerning the infectivity of *S. pertenuis* in the different stages of experimental lesions.

Somewhat similar phenomena have been observed in experimental lesions in syphilis by Brown and Pearce,²³ who have described them in their excellent and comprehensive studies of experimental syphilis

23. Brown and Pearce: J. Exper. Med. **31**:4, 1920.

in the rabbit. We may divert here and dwell on this phenomenon, since it is of interest in the clinical visualization of syphilis and indeed of all spirochetal diseases. The course of syphilis and yaws in the rabbit is somewhat a replica of these diseases as observed clinically. Syphilis and yaws in the rabbit may be mild, transitory and spontaneously cured; again, the lesions may become quiescent or latent, and later active; in this way a cycle is developed. As stated by Brown and Pearce, the duration of this local infection, as in experimental syphilis determined by the presence of active lesions, was as variable as the course of the infection itself, and no fixed limits can be given, either for the several phases of the local reaction or for the infection as a whole. The period of active infection varies from one to more than twelve months. In some animals the entire process was represented by one intense cycle of acute reaction, which terminated within from four to six weeks after inoculation; in others, the infection continued through successive cycles of reaction, but the period of active infection was rarely longer than from two to four months. Brown and Pearce have also shown that *Spirochaeta pallida*, just before the height or relapse of the acute cycle, began to increase in number. This increase continued parallel with the development of the lesions, so that by the time the lesions had reacted to the acme of the first cycle of their development, actively motile organisms were present in large numbers. At this point the organisms suddenly began to lose their motility and to collect in tangled masses; following this phenomenon, they rapidly diminished in number so that within a few days organisms were difficult to find in fluid aspirated from the testicles, and those seen were either degenerated or showed slight motility; in many instances no organisms could be found. After passing through a crisis such as this, actively motile spirochetes again appeared in the testicular fluid and increased in numbers, thus presaging a renewed activity on the part of the lesions. These parallel changes continued throughout the existence of the local infection.

As noted, we have observed in a general way a similar cycle with *Spirochaeta pertenuis*, although our observations have not been sufficiently extensive to formulate an exact comparison. Brown and Pearce attribute the phenomena referred to above to a cyclic immunologic reaction. They have further shown that the infecting power of the organism at this stage is markedly diminished. In one of their experiments, a series of animals inoculated with approximately ten times the dose of immobilized and agglomerated organisms that was used in the controls, showed an incubation period of six weeks as contrasted with three weeks in the controls, while the lesions were as slow to develop and were less pronounced than in control animals.

Similar observations as to the inactivity of *S. pallida* at different periods of the infection were made, and there is no doubt in the minds of these workers as to the significance of the cyclic reactions they describe.

SCROTAL LESIONS IN THE RABBIT

As stated, we failed to produce lesions of the scrotum. Nichols,²² however, succeeded in producing such lesions. He inoculated seven animals under the skin of the scrotum with testicular tissue. In six days two animals had developed hard nodules which enlarged to typical chancres; the other five failed to show lesions. He observed eight chancres after inoculation of the testicle in other animals. The incubation period of these chancres averaged twenty-three to twenty-five days, a period less than half that in syphilis in Nichols' experience. He points out that in contrast with the difference seen in yaws and syphilitic lesions of the monkey's eyebrows, there is practically no difference in the lesions which are produced in the rabbit's scrotum by *S. pallida* and *S. pertenuis*, except as regards the incubation period.

INTRAVENOUS INOCULATION OF RABBITS

As already mentioned, we failed to inoculate rabbits by the intravenous injection of the patient's blood with yaws. Castellani²⁴ produced a generalized infection in rabbits by intravenous inoculation. He says that the character of the lesions produced, which occur mostly about the head, are distinctive of yaws to such an extent that this method may be used in differentiating *S. pertenuis* from *S. pallida*.

EXPERIMENTAL LESIONS IN MONKEYS

Neisser, Baermann⁵ and Halberstädter²⁵ and others—Prowazek, Castellani, Nichols, Levaditi, Ashburn and Craig—have shown that monkeys are susceptible to experimental infection with yaws. The character of the lesions resulting at the site of inoculation, usually the eyebrows, is distinctive; at first it is an infiltrated area which slowly increases in size; there is free secretion of serum that forms into a thick crust, which on removal exposes a granulating red surface. This lesion closely resembles the fungating yaws lesion seen in man.

In the low class of monkeys of the genus *Macacus* and the genus *Semopithecus*, the eruption is confined to the site of inoculation, although *Spirochaeta pertenuis* has been demonstrated by Castellani²⁶

24. Castellani: Biochim. e terap. sper. **8**:337, 1912.

25. Halberstädter: Arb. a. d. k. Gesndhts amte **26**:48, 1907.

26. Castellani: J. Hygiene **7**:558, 1907.

in the spleen and lymphatic glands, thus giving evidence of a generalization of the infection. However, Halberstädter succeeded in obtaining a general eruption in ourang-outangs.

We made several unsuccessful attempts to inoculate the eyebrow of a *Semopithecus* monkey. Nichols²⁷ gives the following differen-

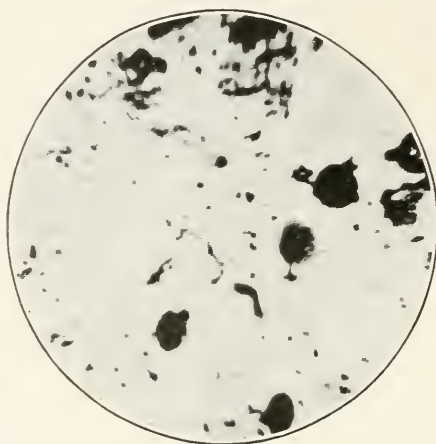


Fig. 10.—*S. pertenuis* stained with anilin black (Rosenberger and Fanz).

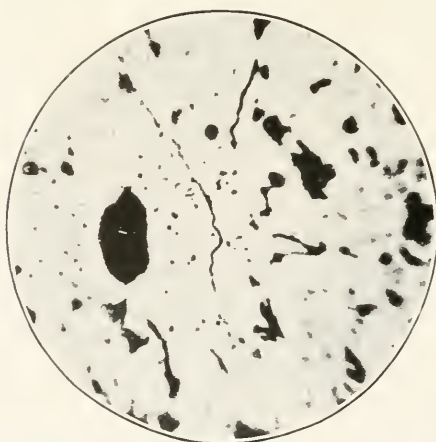


Fig. 11.—*S. pertenuis* stained with anilin black. Note the irregular curves.

tiation between the experimental lesion of yaws and syphilis in the monkey: In yaws the incubation period is from two to three weeks; the lesion is elevated, slightly scaly and edematous. In syphilis the incubation period is about four weeks; the lesion is flat, dry and scaly.

27. Nichols: J. Exper. Med. **12**:621, 1910.

LABORATORY DIFFERENTIATION OF YAWS AND SYPHILIS

Neisser, Baermann and Halberstädter have shown that monkeys infected with yaws do not become immune to syphilis, and vice versa, monkeys infected with syphilis do not become immune to yaws. This experiment furnished further proof that yaws and syphilis are different diseases. In addition, it furnished a definite laboratory method of differentiating the two organisms. It becomes apparent from data herein presented that a laboratory diagnosis of yaws and syphilis is difficult. The diagnosis cannot be made by the Wassermann reaction or the dark field microscope. The rabbit's testicle is not suitable for the resistance experiment of Neisser, Baermann and Halberstädter for the following reasons: We have frequently observed, and it has also been observed by others, that there is a migration of

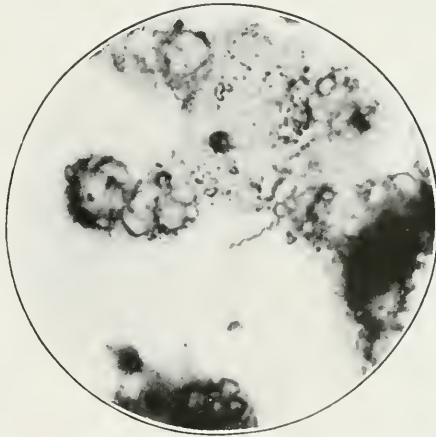


Fig. 12.—*S. pallida* stained with gentian violet.

spirochetes from an inoculated testicle to the noninoculated testicle. In addition, inoculation with *Spirochacta pallida* or *S. pertenuis* does not give a positive result in 100 per cent. of cases. However, Nichols²⁸ succeeded in differentiating the two organisms by testicular inoculation and cross infections with syphilis and yaws after treatment with arsphenamin. He observed that rabbits infected with *Spirochacta pertenuis* were permanently cured by a dose of 0.0045 gm. of arsphenamin per kilo, while animals infected with *S. pallida* and treated with a similar dose usually had a relapse; a smaller dose than 0.0045 gm. per kilo, however, failed to kill *S. pertenuis*.

Nichols treated syphilitic rabbits with 0.01 gm. of arsphenamin per kilo; fifteen days later he inoculated them with yaws. All the

28. Nichols: J. Exper. Med. **14**:209, 1911.

animals became infected with yaws, although the testicular lesions were smaller than normal and the incubation period longer. Other syphilitic animals were similarly treated and reinoculated with syphilis, thirteen to sixteen days after treatment. None of the animals became infected with syphilis. Hence, Nichols concludes that in rabbits, as well as in monkeys, a difference between the two diseases can be demonstrated by inoculation and curative experiments.

Although our observations regarding arsphenamin and neo-arsphenamin therapy in experimental yaws are not yet completed, we failed to cure rabbits infected with *S. pertenuis* with 0.005 gm. of arsphenamin per kilo, a slightly greater dose than that which, in Nichols' experience, cured permanently. Contrasted with the dose of arsphenamin, we observed the curative dose of neo-arsphenamin to be 0.008 gm. per kilo.

The most reliable and convincing method of differentiating between yaws and syphilis, by laboratory experiments, is the production of a chancre on one eyebrow of a monkey and the subsequent production of a frambeside on the other eyebrow or vice versa.

THE WASSERMANN REACTION IN HUMAN AND EXPERIMENTAL YAWS

Judging from the occasional reports in literature in which the Wassermann reaction in yaws was negative, it is evident that the test is not invariably positive. In Baermann and Wetter's²⁹ series of 125 cases of yaws studied in Java, the Wassermann reaction was positive in thirty-five of thirty-eight acute untreated cases. In ten treated cases the reaction was positive in six. In fourteen cases of latent yaws, in which the infection was of many years' duration and a long time had elapsed without symptoms or treatment, the reaction was positive in five.

According to Schüffner and Violle, the complement fixation reaction is frequently positive if an alcoholic extract of syphilitic liver is used as an antigen, while there is no fixation if an aqueous extract is used. It may be recalled that the original Wassermann technic provided for the use of an aqueous extract of syphilitic liver. When one contrasts the relative merits of these two antigens when used in the Wassermann reaction in syphilis, it becomes consistent with the experiment of Schüffner and Violle that an antigen of an alcoholic extract of syphilitic liver should give a greater percentage of fixation in yaws than an antigen of an aqueous extract of syphilitic liver.

The Wassermann reaction³⁰ of the serum of the patient with yaws was performed with the following three antigens: a 4 per cent. cholesterolized beef heart, alcoholic syphilitic liver and acetone insoluble

29. Baermann and Wetter: München. med. Wchnschr. **57**:2131, 1910.

30. The Wassermann tests were kindly performed for us by Prof. John A. Kolmer.

lipoids. In the acute untreated stage the reaction was ++++ with all antigens; however, after treatment the reaction with the cholesterolized antigen inhibited hemolysis to a greater degree; in other words, was stronger than the reaction performed with the remaining two antigens. The last reaction we observed was ++ with the cholesterolized beef heart antigen and negative with the other two antigens. It is interesting to note that the relative sensitiveness of these three antigens when used in the Wassermann reaction in yaws is the same as in our experience with syphilis.

The complement fixation test of the yaws serum was also performed with a salt solution extract of a testicular nodule from a rabbit infected with yaws.³¹ This extract contained about three *S. pertenuis* organisms to a microscopic field. The reaction with the

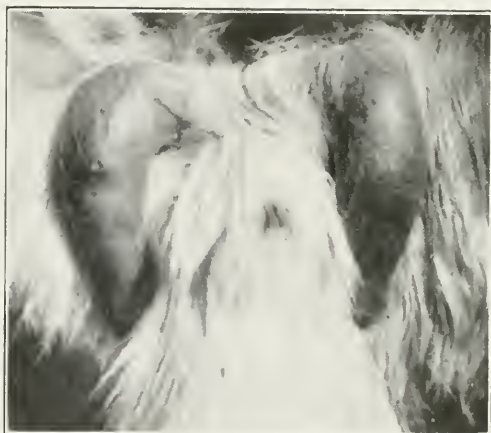


Fig. 13.—Rabbit's testicles successfully inoculated with *S. pertenuis* from cutaneous lesions in the case reported. The organs are enlarged and edematous; a palpable node is present in each organ. A dark field examination of the serum obtained on puncturing each node disclosed many spirochetes.

yaws serum yielded a slight, but definite, degree of fixation, whereas the reaction of the pooled serums of three syphilitic patients yielded separately a ++++ reaction with a cholesterolized, alcoholic, syphilitic liver and acetone insoluble lipid antigens. From this observation it would appear that the Wassermann producing substance in yaws, as in syphilis, has a dual origin; on the one hand, it is a specific biologic substance caused by *S. pertenuis* and *S. pallida*, respectively,

31. It should be noted that salt solution was used in making this extract. Specific culture antigens employed in the complement fixation tests have been made by some investigators using alcohol as an extracting agent, but Dr. Kolmer believes that a salt solution extract gives better results.

and on the other hand, a nonspecific substance arising less directly from these organisms.

The complement fixation reaction obtained in human yaws serum stated above, using a specific yaws antigen, is in accordance with similar results obtained by Castellani³² and by Bowmann;³³ on the other hand, Baermann and Wetter³⁴ failed to obtain fixation in the serum of human yaws using a specific yaws antigen. Nichols³⁵ failed to obtain fixation with the serum of animals infected with yaws with a specific yaws antigen. He applied complement fixation tests to the serums of rabbits infected with *S. pallida* and *S. pertenuis*, in which he used culture antigens of these two organisms, as well as culture antigens of *Spirochaeta dentium* and a syphilitic liver antigen. He showed that rabbits infected with *S. pallida* and with *S. pertenuis* gave a ++ reaction with the syphilitic liver antigen, but no reaction with specific culture antigens either at the height of the lesions or after recovery.

The nature of the substance producing a positive Wassermann reaction in yaws is not definitely known; indeed, the underlying principle of this reaction in syphilis is not definitely known. We do know, however, that the Wassermann producing substance is of lipotropic nature, and that the character of the reaction is probably colloidal. That this substance is apparently not a specific biologic product of spirochetes is evidenced by the fact that the same, or at least a similar substance, is present at times in leprosy.

It will be recalled that weak complement fixation occurs with a small percentage of serums in human syphilis employing a specific antigen, that is, a culture of *S. pallida* or aqueous extracts of infected testicles. This observation, as already mentioned, points to a dual origin of the Wassermann producing substance in syphilis. However, this antigen is considerably less sensitive than the nonalcoholic extracts of syphilitic and nonsyphilitic tissue now in common use and therefore of no practical value in the conduct of the Wassermann test. Indeed, the more frequent and greater fixation obtained with nonspecific antigens is proof that the Wassermann test is not a specific antibody complement reaction. The complement fixation test with specific antigens, that is, aqueous (not alcoholic) extracts of pure cultures has not a sufficiently definite status to be of great value in the differentiation of yaws and syphilis; although our observations in this regard were positive, the observations of others were variable.

32. Castellani: J. Hygiene **7**:558, 1907.

33. Bowmann: Philippine J. Sc. **5**:485, 1910.

34. Baermann and Wetter: München. med Wchnschr. **57**:2131, 1910.

35. Nichols: J. Exper. Med. **14**:198, 1911; South. M. J. **5**:528 (Sept.) 1912.

There is a paucity of data in the literature concerning the persistency of the Wassermann reaction after the disappearance of yaws lesions following treatment. Many writers record the rapid disappearance of lesions following arsphenamin therapy, but make no mention of the behavior of the Wassermann reaction in these cases. For example, Rost³⁶ has reported that of 500 cases of yaws eighty-one, 8 per cent., were cured by the intramuscular injection of arsphenamin, 15 per cent. with two, and the remainder with three injections. In the light of the Wassermann studies in our case we can only regard such cases as a clinical cure. Indeed, it is a commonly accepted belief that Ehrlich's unfulfilled hope of accomplishing a therapeutic sterilisans magna with one injection of arsphenamin in syphilis is accomplished in the arsphenamin therapy of yaws. There is no doubt that yaws is more easily cured than syphilis, and that one injection of arsphenamin is considerably more potent than in syphilis.

Baermann and Wetter have observed that the Wassermann reaction may disappear in yaws after two or three injections of salicylate of mercury. After treatment there may be a clinical recurrence. This possibility, however, is considerably less than in syphilis. Both Strong³⁷ and Castellani³⁸ have reported recurrences after treatment with doses of 0.3 to 0.4 gm. of arsphenamin, although these recurrences were in a small percentage of the total number of cases treated. A therapia sterilisans magna may be accomplished in yaws with more certainly than in syphilis, but not in all cases, even though there is a disappearance of all lesions. In the light of modern knowledge it is erroneous to regard such cases as necessarily cured.

The persistency of the Wassermann reaction in our case suggests that yaws may continue for some time in an asymptomatic stage after complete disappearance of all the cutaneous lesions in a manner similar to that which occurs in syphilis. This receives confirmatory support from the experience of Castellani, who states that oral treatment should be prolonged for a long time after the complete disappearance of the eruption. As clinical experiments on inoculated monkeys prove that the specific spirochetes may and do persist in the lymphatic glands and internal organs long after the cutaneous manifestations have disappeared.

DISCUSSION

DR. FORDYCE stated that a case of yaws was brought to his clinic last winter from the Naval Hospital in Brooklyn. The patient was an American sailor who had been stationed at Brest, where he came in contact with sailors from all over the world. He had lesions similar to those mentioned by Dr.

36. Rost: München. med. Wchnschr. **59**:924, 1912.

37. Philippine J. Sc. **5**:433, 1910.

38. Castellani: Arch. f. Schiffs.-u. Tropen.-Hyg. **15**:11, 1911.

Schamberg. Professor Lindenberg of Sao Paulo, Brazil, who was visiting the clinic at that time, readily diagnosed the case as yaws. This was confirmed by the easy determination of the spirochetes under the dark field microscope. The Wassermann reaction was strongly positive. Dr. Fordyce suggested that as Professor Lindenberg was present at the meeting he be asked to tell the Association something regarding the distribution of yaws in Brazil.

PROFESSOR LINDBERG said that he could not avail himself of the invitation to any great extent because he did not speak well in English, but the exposition of Professor Schamberg seemed very complete. He believed he had done all which should be done in the case, and he could only emphasize that in Brazil the most interesting thing was the comparison with syphilis. In Brazil they attached great importance to the difference in the location of the spirochete in the tissue in the two diseases. In yaws the spirochete was always found in the connective tissue; in syphilis, on the contrary, the spirochete is not found in the connective space. When the organisms were found in the miliary abscesses which formed, they were considered specific of yaws.

DR. HIGHMAN was particularly interested in the histologic picture thrown on the screen. He had seen the case Dr. Fordyce described and the histologic material from it. Unfortunately, the technician was ill during the time the Levaditi stain was being prepared, and it was not successful, but the general morphology was particularly interesting. The only striking difference between that specimen and this one was in the tremendous number of plasma cells in the infiltration. He understood from Professor Lindenberg and from the literature that there was a larger number of plasma cells in yaws than in syphilis, and there were much less marked vascular changes. It was the first case of yaws he had ever seen, but he gathered that it was a typical morphologic demonstration of the disease.

DR. RAVOGLI said that when visiting in Florence in the clinic of Prof. C. Pelliszori he saw a case of yaws in a man who had worked for many years in St. Paul of Brazil. He had a papular eruption all over the body, but the nose and palate were most seriously affected, the palate being nearly destroyed. Dr. Ravogli had read of several cases reported by Dr. Splendore, who was working with Castellani. It is a horrible disease, but arsphenamin treatment has diminished its destructiveness.

DR. POLLITZER stated that he was indebted to Dr. Schamberg for an account of his case and photographs, which he submitted to him after seeing the patient. The case had impressed Dr. Pollitzer as being one of yaws rather than syphilis. In addition to the many points brought up by the paper, he was struck with the location of the lesions. The fact that the man had for two months some systemic disorder of an indefinite type was important. If this had been syphilitic fever, the eruption would have appeared within two or three months after his infection. But the kind of eruption which the patient showed did not occur in syphilis so soon after infection and, above all, it did not present the distribution seen in this case. On the other hand, this was just the sort of eruption that one found in yaws. The preliminary period of incubation in which the patient had malaise and rise of temperature, followed by a spirochetal eruption of a character which was not like that of syphilis, spoke strongly in favor of yaws.

In the second place, the extremely rapid disappearance of the lesions after arsphenamin treatment was also characteristic of yaws. It was interesting to recall that in Batavia, where there formerly had been several large hospitals

devoted entirely to the treatment of yaws, these hospitals had been closed or devoted to some other purpose within a month after the introduction of arsphenamin treatment. The condition cleared up so rapidly under arsphenamin treatment that the treatment of yaws had become ambulatory.

DR. SCHAMBERG, closing, said he was particularly interested and pleased to learn from Professor Lindenberg that he regarded the finding of the spirochetes in miliary abscesses in the epidermis as indicative of yaws. Curiously, no such statement is made in Castellani's last book, in which there is a most excellent description of the disease from the clinical and pathologic side. No mention of the occurrence of miliary abscesses and the suggestive localization of the spirochetes in such abscesses is made.

A point of general interest is the fact that Ehrlich's hope of a *therapia sterilizans magna*, which has failed in syphilis, is apparently achieved in yaws. From the descriptions of various writers, the spirochetes of yaws differ as much from each other as from the spirochete of syphilis. Some contend that it is thicker than the *S. pallida* and others that it is thinner. Noguchi described several types of *Spirochaeta pallida*, one of which was thick and the other thin. Dr. Schamberg thought no one would attempt to differentiate the spirochete of yaws from that of syphilis on morphologic grounds alone. It was interesting that the spirochetes of yaws were largely exterminated by one dose of arsphenamin, while in syphilis this is not true.

DR. WILE asked whether the cultures under anaerobic conditions were negative.

DR. SCHAMBERG, replying to Dr. Wile, said that up to the present time the cultures under the strictest anaerobic conditions had been negative, but they were persisting in their efforts to cultivate the organism from the testicular material, and they hoped to achieve a successful result. He was under the impression that Noguchi had successfully cultivated the organism of yaws in culture. He thought it significant that this organism had failed to take stains in smears which *Spirochaeta pallida* took readily. Many writers had referred to the fact that the yaws' spirochetes were difficult to stain.

PROFESSOR LINDENBERG stated that during the time of slavery in Brazil, thirty or forty years ago, this disease was common among the slaves. After the slaves were made free and the hygienic conditions were improved it became a rather rare disease in Brazil. In the course of a year he would perhaps see only two or three cases. In his opinion improvement resulted not from the use of arsphenamin, but from the better hygienic conditions of the people and the fact that there was not so much chance for contagion as in the days of slavery when many of these people were crowded together in one room.

Abstracts from Current Literature

UEBER DEN EINFLUSS VON QUECKSILBER BEI VERSCHIEDENER DOSIERUNG AUF DIE SPIROCHAETENWUCHERUNG IM MENSCHLICHEN KOERPER (CONCERNING THE EFFECT OF MERCURY AND ARSPHENAMIN IN VARIOUS DOSES ON THE PROLIFERATION OF SPIROCHETES IN THE HUMAN BODY).
W. SCHOLTZ and KELCH, Arch. f. Dermat. u. Syph. **123**:855, 1916.

The authors have previously frequently expressed the opinion that mercury has no direct lethal effect on the spirochetes of syphilitic lesions when administered by injection irrespective of the preparation (soluble or insoluble) used. They report in this communication an attempt made to learn whether mercury given intensively, even almost to the danger point of toxicity, would give better results. Mercury was administered according to the following scheme:

Month	Day	Hour	Dose	Mercuric		Mercuric	
				Chlorid	or	Salicylate	or Calomel
1	1	9	I	0.01-0.02		0.05-0.06	0.04
		3	II	0.01-0.02		0.05	0.04
	2	9	III	0.01		0.05	0.04
		3	IV	0.01		0.05	0.04
	3	9	V	0.01		0.05	0.04
		3	VI	0.01		0.05	0.04

With this type of treatment there was no quicker destruction of spirochetes than with the ordinary procedure. The clinical lesion regressed slightly more rapidly, and the proliferation of the spirochetes was reduced parallel with it. These observations tended to uphold the idea that mercury has only an indirect effect on spirochete proliferation through the cells and serums of the body.

At the close of this series, the authors studied the effect of various doses of arsphenamin on the proliferation of spirochetes. It was their object to learn the smallest amount of arsphenamin that, given at one dose, would give the greatest effect on the proliferation of the spirochetes in papules and patches, and then to learn if the same dose divided into three or four partial doses would have a more or a less active effect on these manifestations.

Further experimentation justified the conclusion that 0.2 gm. of arsphenamin gave the effect desired. Negative findings for the spirochete were reported only after the examination of twenty fields of the dark field had been studied. (In all the experiments, neo-arsphenamin in equivalent dosage was used.)

Eleven patients with active lesions were studied. Arsphenamin was given in the following manner, and dark field examinations positive in every instance prior to the first injection were all negative within twenty-four to forty-eight hours. Typical protocol:

RESULTS OF ARSPHENAMIN IN CONDYLOMAS ABOUT ANUS AND PATCHES OF THROAT

Date	Condylo-	Mucous Patches
	Spirochetes	
1/ 9	Positive	Positive
1/10	Positive	Positive
1/10 a. m., arsphenamin, 0.05 gm.....		
1/11 p. m., arsphenamin, 0.05 gm.... Evening	Negative	Positive
a. m., arsphenamin, 0.05 gm.....		
1/12 p. m., arsphenamin, 0.05 gm.... Evening	Negative	Negative
1/13	Negative	Negative

Thereafter injections were given as follows:

9 a. m.....	0.2 -0.25 gm. arsphenamin
1 p. m.....	0.25-0.3 gm. arsphenamin
Next day 9 a. m.....	0.3 gm. arsphenamin

The doses after the first dose were given only if no ill effects followed. The urine was examined for albumin before each injection, and the quantity was also determined for each interval. Bowel movements were insisted on. The diet was restricted, and alcohol and tobacco were interdicted. After each injection the patient was brought into a light sweat by a hot pack for from one to two hours.

The success of this method has seemed so remarkable that the authors have decided to maintain about the same routine. Many of their patients had been under observation for five and six years. The primary cases have never shown a recidive lesion, although in many treatment was instituted when the Wassermann reaction was positive. From about 85 to 90 per cent. of patients with secondary cases have been cured. The patients included in this estimate had received but one course. If the patients receiving a second course were added, the percentage of cures would be over 95.

The following short bibliography may prove of interest to those seeking further information:

Altman: *Dermat. Ztschr.* **23**:257, 1916 (contains bibliography).

Scholtz: *Deutsch. med. Wchnschr.* **39**:1441, 1913; *ibid.*, *Ztschr. f. Dermatol.* **22**:249, 1915.

Pollitzer: *J. Cutan. Dis.* **34**:635, 1916.

Hazen: *Am. J. Syphilis* **2**:778, 1918.

Goodman: *Am. J. Syphilis* **3**:449, 1919; *ibid.* **3**:661, 1919; *ibid.*, *New York M. J.* **112**:494, 1920.

Ormsby: *J. A. M. A.* **75**:1, 1920.

GOODMAN, New York.

RODENT ULCERS AND ALLIED GROWTHS: AN ANALYSIS OF SIXTY AUSTRALIAN CASES. J. BURTON CLELAND AND NORMAN PAUL, M. J. Australia **1**:407, 1920.

The authors state their belief that in spite of the uniformity of the origin of cells and their presumed equality of potentialities their ultimate highest development depends on the structures among which they find themselves and their situation in relation to the whole body. They believe that the transplantation of the chorionic villi to a denuded surface, for example, after the manner of a skin graft, might lead to successful "take" with the formation of squamous epithelial surface. In their opinion, therefore, the cells of the active parts of the various structures (appendages) of the skin (cells of the pilosebaceous glands and basement layer of the epidermis) have in many cases not entirely lost all their potentialities in forming other structures. Thus the basement layer may still be able to form pilosebaceous glands and cells of the pilosebaceous glands may in their turn be able to form squamous cells. They believe also that on account of the position of the cells such potentialities are suppressed, but that under certain circumstances expression may be given them. The more remote the cell is ontogenetically from these types of structures and the more specialized are its services, the less likely is the expression to be clear and distinct. Thus they find in squamous cell epitheliomas (though in exceptional cases) plasmodial-looking masses which might possibly be interpreted as representing the syncytial covering of the villi. The cells forming the surface epithelium

have less specialized work, and the authors believe that is the reason of the great diversity in behavior of new growths derived from this. They believe they can trace, not only squamous epitheliomas, to the surface epithelium, but also to certain growths resembling rodent ulcers, which they believe are derived from pilosebaceous apparatus.

They, therefore, group epitheliomas into two divisions which, however, grade one into the other—at one end the typical rodent ulcers and at the other typical squamous epitheliomas with well marked cell nests.

1. Typical basal cell epitheliomas usually derived, they believe, from pilosebaceous apparatus comprising clinically and histologically typical rodent ulcers.

2. Atypical basal cell epitheliomas derived from the basal cell layer. They closely resemble the preceding, the cells usually being larger, mitoses more frequent and the concentric arrangement more evident, while the cell masses are irregular and ill-defined, usually without any definite marginal palisade layer.

3. Atypical squamous epitheliomas, comprising undoubted squamous epitheliomas, but in an almost incomplete absence of cell nests clearly indicating a relationship with the rodent type.

4. Typical squamous epitheliomas.

5. Several anomalous growths are also included in this group.

The authors then cite several cases to support their histologic findings.

GUTIERREZ, Manila.

UEBER SILBERSALVARSAN (EIN BEITRAG ZUR FRAGE DER GLEICHZEITIGEN KOMBINIERTEN QUECKSILBER-SILBERSALVARSANTHERAPIE) (SILVER ARSPHENAMIN [A CONTRIBUTION TO THE PROBLEM OF SIMULTANEOUS COMBINED MERCURY-SILVER ARSPHENAMIN THERAPY]). *L. ARZT, Dermat. Ztschr.* **31**:165, 1920.

The first part of this paper deals with the problem of the value of mercury in the arsphenamin treatment of syphilis. Mercury was reintroduced into the treatment plan when the failure of Ehrlich's "Therapia magna sterilisans" was certain. Whether mercury is essential with the modern plan of injection of the Ehrlich compounds has aroused discussion among therapeutists, who have divided themselves into two classes: one that believes the combination is harmful and one that believes the combination is necessary for success in the therapeutic attack on the disease. Wechselmann, Gennerich, Dreyfuss, Notthafft and others oppose the simultaneous injection, and Kerl, Goldberger and others sponsor the combination treatment.

Since the introduction of "silver arsphenamin" by Kolle, a new factor has entered the discussion. Is it possible that the combination of silver and arsphenamin equals the mercury-arsphenamin combination, and would the three metals, mercury, silver and arsenic, if injected simultaneously, be too much for the organism to eliminate without causing damage?

Silver arsphenamin alone had already been injected by Kerl in a series of cases, but recurrent lesions made their appearance, which led Arzt to formulate this schema:

Silver arsphenamin is injected at twenty-four hour intervals in dosage of 0.15, 0.2 and 0.25 gm. thrice repeated, one week apart. Simultaneously, mercury inunctions are given: eventually injections of soluble cyanid (fifteen treat-

ments) or insoluble salicylate 10 per cent. (eight or ten treatments). The selection of the twenty-four hour interval is accredited to Notthaff, who is said to have used the method for many years.

Arzt treated 53 patients, of whom 16 had primary syphilis; 12 of these were male and 5 female; 37 had secondary syphilis; of these, 12 were male and 25 were female.

He is able to say that the disappearance of *Spirochaeta pallida* from the lesions and the clearing of infectious manifestations is rapid and compares favorably with the old arsphenamin treatment, perhaps being even slightly more rapid in its action. Although Arzt has seen no recurrent lesion, he has not observed the cases long enough to state definitely that these do not appear, and he says that conclusions in this regard are not and cannot be drawn. The blood reaction has been negative after the course of treatment as outlined, except in one case in which the patient had alopecia and gave a positive Wassermann reaction. Of all the patients giving a negative reaction at the end of the treatment, not one had developed a positive reaction since the cessation of treatment. This is thought to be significant. Of course, permanent results will not be known for years.

By effects and ill effects were rare. Angioneurotic syndromes, rise in temperature, icterus and exanthem were encountered only occasionally and were exceedingly mild. Why one patient should develop icterus and all the others should escape remains to be discovered.

Silver arsphenamin is thought to be an exceedingly efficient addition to the armamentarium of the syphilologist.

GOODMAN, New York.

A CONSIDERATION OF CERTAIN ASPECTS FOR PROTEIN HYPER-SENSITIVENESS IN CHILDREN. K. D. BLACKFAN, Am. J. Med. Sc. **160**:341 (Sept.) 1920.

A few case reports are given illustrating the most common forms of sensitization, such as eczema, asthma and urticaria due to substances ingested—milk, eggs, cereal, meats and other foods. Alarming symptoms may occur when the infant is first given some of the provocative substance as this hypersensitiveness may be present at birth, although it may be acquired later or conveyed from the mother.

The author uses the von Pirquet method of skin scarification, expecting the reaction within fifteen minutes, which subsides in the course of the next half hour. The intracutaneous method is more delicate, but the results are more difficult to interpret, especially if the reaction is delayed.

Children are not as a rule sensitive to as many different proteins as adults are, the most common substances used by the writer being egg, milk, cereals and meats, horse serum and dander, timothy, red-top and ragweed.

The author's experience agrees with that of others in that he finds that many patients are sensitized to more than one protein and react accordingly, some even reacting to widely varying substances.

In treatment it is not absolutely necessary to omit all protein as many patients are able to ingest small quantities without harm. Desensitization is the most satisfactory method of procedure, the aim being to enable the patient to eat proteins without reaction and also to secure a negative skin reaction. If the patient reacts to only one protein, that protein should be excluded from the diet, after which desensitization may be begun if desired.

JAMIESON, Detroit.

A FATAL CASE OF LUPUS ERYTHEMATOSUS, WITH AUTOPSY.

R. CRANSTON LOW, W. R. LOGAN and ANDREW RUTHERFORD, Brit. J. Dermat. & Syph. **32**:253 (Aug.-Sept.) 1920.

This interesting case was that of a young woman who, during the four and one-half years in which she was under observation, had four recurrences of lupus erythematosus, all but one accompanied by an elevation of temperature and with complete disappearance of symptoms between attacks, death occurring after the last attack, which lasted about two months. The second attack, unaccompanied by fever, was of the ordinary type of chronic lupus erythematosus, whereas in the other three attacks the eruption was more widespread and diffuse. The temperature did not at any time resemble the swinging type associated with tuberculosis.

Necropsy disclosed a number of pathologic changes, many of them due to a terminal laryngeal diphtheria. The authors say that it is difficult to draw conclusions from the result of the postmortem examination. "The patient undoubtedly suffered from fairly extensive tuberculous lesions; they were not, however, any more extensive than those frequently seen in patients dying of other conditions.

A streptococcus was found in the heart blood at death, but the authors realize that it may have been introduced into the blood shortly before death as a result of the diphtheria. It is possible, however, that this organism may have been responsible for the presence of a subacute pericarditis, evidently nontuberculous. They ask whether it is not possible that the pericardial lesion was a focus from which a streptococcal focus might arise, because these cases of generalized lupus erythematosus, apart from the skin eruption, have many features in common with cases of malignant endocarditis.

SENEAR, Chicago.

EIN FALL VON SOGENANNTER HYSTERISCHER DERMATOSE (A CASE OF SO-CALLED HYSTERICAL DERMATOSIS). C. RASCH, Arch. f. Dermat u. Syph. O. **121**:21 (Feb.) 1915.

The patient was a 17-year old girl from a rural community, with a history of a chronic skin condition of two years' duration. She had been treated by a number of physicians who had made various diagnoses.

She presented about 130 pigmented and excoriated lesions, each from 6 to 7 cm. in length and from 1 to 2 cm. in width. The lesions were on the anterior surface of the body and extremities. Her back and the posterior aspect of her limbs were practically free. The lesions were parallel to each other. Some were light red in color, others dark red and brown. On a few of them there were bloody crusts.

She had marked anesthesia of her entire skin. She finally admitted that she produced the lesions herself by rubbing with a calloused thumb.

HEITHAUS, Cleveland.

THE SAPROPHYTISM OF VENEREAL ORGANISMS AND ITS DANGERS. H. GOUGEROT, Internat. J. Public Health **1**:173 (Sept.) 1920.

Gougerot believes that bacteriologic, clinical and experimental evidence shows that saprophytism of venereal organisms exists. From the point of view of prophylaxis, visceral saprophytism of *Spirochaeta pallida* is important as regards the testicles and salivary glands, for it can be demonstrated that the sperm

may be virulent, even though the testicles appear to be free from disease. He has found "spirochaetae in the mouth or the vaginal mucus of patients who have been treated and apparently cured, so that they have no lesion at the time."

Clinical experiences are cited to show the apparent saprophytism of Ducrey's bacillus, but microscopic proof is lacking.

It is more difficult to prove the existence of the saprophytism of the gonococcus. In the majority of cases which apparently fall into this category there is a latent and deeply concealed gonococcal focus.

At this time he wishes merely to insist on saprophytism as a fact, and to call attention to its great importance in connection with the prophylaxis of venereal disease.

MICHAEL, Houston, Texas.

PAPULO-URTICARIAL RASHES CAUSED BY THE HAIRLETS OF CATERPILLARS OF THE MOTH (EUPROCTIS EDWARDSI NEWN). J. BURTON CLELAND, M. J. Australia 1:169, 1920.

Rashes following the handling of dead wood were first reported to Cleland in March, 1916. At that time no definite cause could be ascertained. However, in November, three of Cleland's children found about half a dozen caterpillars turning into pupas in flimsy cocoons, under the bark, near the base of an apple tree. The dry cast skin of the hairy caterpillars were mixed with the slight weblike cocoons. The children gathered the cocoons and within two minutes the older ones complained of irritation. In a little while urticarial papules could be seen. Next day their necks were covered with hundreds of small papules still irritating. In one of the children, in addition to papules, some edema of the adjacent eyelid appeared. The papules disappeared in the course of a few days. When the webbing of the cocoons was examined, numerous spicules were found entangled in their threads. The cocoons were sharp-pointed, acuminate, with a central cavity as if filled with air in mounted specimens. The webbing containing the hairlets was acid to litmus paper, and Cleland is of the opinion that the acid was formic acid.

GUTIERREZ, Manila.

UEBER EINEN FALL VON POSTEXANTHEMATISCHER HAEMATOGENER TUBERCULOSIS CUTIS VERRUCOSA MIT PIGMENT-HYPERTROPIEN (CASE OF HEMATOGENOUS TUBERCULOSIS VERRUCOSIS CUTIS WITH INCREASED PIGMENT FOLLOWING EXANTHEM). MARTIN SILBERSTEIN, Arch. f. Dermat. u. Syph. 123: 863, 1916.

A man, 41 years old, who did not have tuberculosis, had measles at the age of 14. Following this exanthem he suffered with pulmonary disease, chronic inflammation of the left elbow joint and chronic inflammation of the skin of different localities in the following order: left elbow, neck, right elbow, buttocks. Warty formation, in the course of the process, regressed leaving thin white scars and occasional areas of increased pigmentation. The lung condition became more serious and the patient died. The skin changes, from their clinical and histologic aspects, were those of tuberculosis verrucosis cutis. The suprarenals did not disclose any lesions on histologic examination, and the case cannot be identified with Addison's disease. The pigmentation is thought to be the result of the extremely chronic course of the disease (over twenty-five years).

GOODMAN, New York.

DERMATOLOGIC ABSTRACTS

JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION

ARGYRIA FOLLOWING INJECTIONS OF SILVER ARSPHENAMIN.
LOCHTE, Therap. Halbmonatsh. **34**:334 (June 15) 1920.

Lochte reports a case in which a young woman of 21, who had contracted syphilis for the first time, received seven injections of neo-arsphenamin, whereupon all manifestations disappeared within eight weeks. A relapse occurred ten months later, at which time the diagnosis was: syphilis nodosa of the scalp; gummatous periostitis of the tibia; syphilitic ulcer on the right arm. Some of the ulcers were fresh, some were scarred over, with distinct marginal infiltration. She was referred to a specialist. A month later she reappeared and stated that she had consulted a specialist, who gave her twelve injections of silver arsphenamin. The first injection was given intramuscularly, simultaneously into the right and left buttocks (0.2 gm.). There was no special pain. Five days later icterus appeared, which lasted fourteen days. Treatment was, however, not discontinued, as the patient felt well. A few days later, the patient noticed for the first time an ashen gray discoloration of the skin, which rapidly became more marked. When last seen the skin of the face and body presented a steel-gray color, which gave a peculiar impression. Even the eyes showed the same color. There were no outward manifestations of syphilis. Lochte did not see the case himself. Sweating treatment and homeopathic remedies, self-prescribed, were of no avail.

NEUROSYPHILIS INVESTIGATION OF MASSACHUSETTS COMMISSION ON MENTAL DISEASES. O. J. RAEDER, *Am. J. Insan.* **76**:449 (April) 1920.

A complete recovery mental, physical, and laboratory, after less than five years or ten years or even before death Raeder says may be questioned. An apparently recovered neurosyphilitic may show none of the above signs or findings, yet at necropsy following intercurrent disease of senility, a focus of inactive treponemas may be found to occupy a circumscribed area somewhere in the brain, just as is commonly found an area of fibrosis or calcification in the lungs, the scar of a healed tuberculosis. In 428 cases of neurosyphilis treated during a period of four years, 129 cases or practically 30 per cent. showed definite benefit. One hundred and twenty-five patients are under treatment in hospitals of which a certain percentage can be expected to show similar improvement. The relatives (spouses, parents, offspring) of syphilitics and neurosyphilitics form a most important group in which not only syphilis but the earliest degrees of neurosyphilis, in the presymptomatic, often entirely unsuspected stages, are brought to light by lumbar puncture and sero-analysis. It is in these types that by far the most benefit can be expected.

NEUROSYPHILIS AND PSYCHOSES. L. G. LOWREY, *Arch. Neurol. & Psychiat.* **3**:500 (May) 1920.

Nineteen cases are presented by Lowrey of which fourteen were undoubted cases of neurosyphilis, one case of pseudoparesis and four had negative physical and equivocal serologic findings. Of the fourteen undoubted cases only four presented clinical evidence from which a diagnosis of neurosyphilis could be made. Since neurosyphilis may exist in association with any type of mental symptoms, and since such states may exist in the absence of any of the usual signs and symptoms of neurosyphilis, Lowrey urges that lumbar puncture should be done at least in all cases which present any atypical features. It is equally important to puncture in cases with any clinical signs of neurosyphilis, since the signs may be misleading.

PATHOGENESIS OF EPITHELIOMAS. IV. K. YAMAGIWA and K. ICHIKAWA, *Mitteilungen a. d. med. Fak. d. kais. Univ.*, **22**:1 (Aug. 28) 1919.

The Journal has mentioned from time to time the success of Yamagiwa and Ichikawa in inducing the production of epitheliomas by painting the rabbit ear with tar. They here report similar research on the mammary gland. In 6 per cent. of 47 cases, repeated application of a tar-lanolin mixture was followed by changes in the tissues, as they show in ten handsome plates, which are of an unmistakable adenochancroid or carcinoma type. Their research is being continued with the aid of the Japanese Cancer Research Society and a special grant from the government. They say that they have never learned of an instance of spontaneous mammary cancer in rabbits. They injected subcutaneously 1 c.c. of the mixture of lanolin and an aqueous extract of tar, twice a month and later once a month, or the injection was made with 0.3 c.c. of pure tar directly into the mammary gland once a month. The rabbit with the adenochancroid cast four litters during the 463 days of the experiments.

TARDY HEMIPLEGIA IN SYPHILITICS. H. VEDSMAND, *Ugesk. f. Læger* **82**:1077 (Aug.) 1920.

Vedsmund relates that there was a history of syphilis in 15 per cent. of 81 patients with hemiplegia that had developed after 60. He knows of only one publication on the connection between hemiplegia and syphilis since the Wassermann test was introduced. This one article is H. A. Thomas' monograph on 740 cases of hemiplegia; he found syphilis in 11 per cent. of those in the forties; 7 per cent. in the fifties (Vedsmund, 12.5 per cent.); 13 per cent. in the sixties (Vedsmund, 25.7 per cent.), and none beyond this, while Vedsmund had 8.8 per cent. in the seventies.

JAUNDICE FOLLOWING NEO-ARSPHENAMIN TREATMENT. H. H. SILBERGLEIT and FÖCKLER, *Ztschr. f. klin. Med.* **88**:333, 1919.

Silbergleit and Föckler relate that in the winter of 1917-1918 they had thirteen cases of acute yellow atrophy of the liver, all fatal, and all occurring in syphilitics who shortly before had been given mixed mercurial and neo-arsphenamin treatment. In eight other cases severe jaundice developed, but the men recovered. Weil's disease could be excluded, but nothing could be found to explain these cases. A fourteenth case of atrophy developed outside but it was not known whether the man had been taking treatment or not.

FATE OF CHILDREN OF SYPHILITICS. MARIE KAUFMANN-WOLF and EMMY ABRAHAMSON, *Ztschr. f. klin. Med.* **89**: 274, 1920.

This article reports the fifth series of the kind, including 213 living children of syphilitic parents. The total mortality for the entire five series was at least 70 per cent. when the mother was infected, and under all conditions it was about 50 per cent. The morbidity of the living averaged 50 per cent., so that only 25 per cent. of the children in the 134 families grew up healthy.

GENERAL PARESIS AMONG ARABS. A. POROT and N. SENGÈS, *Ann. d. méd.* **6**:444 (Jan.) 1920.

The total absence of general paresis among Arab syphilitics has long attracted attention. Not even the stress of years of service at the front brought any tendency to general paresis among the Arab troops. Porot and Sengès relate that in their experience at Algèr, notwithstanding the extreme prevalence of syphilis, they have never encountered but one instance of general paresis, and this was of such a mild form that the Arab officer was able to serve for more than three years at the front, and the necropsy findings were meager.

Society Transactions

NEW YORK ACADEMY OF MEDICINE, SECTION ON DERMATOLOGY AND SYPHILIS

DR. JOHN E. LANE, *Chairman*

Regular Meeting, Oct. 5, 1920

VERRUCAE OF FEET. Presented by DR. TRIMBLE.

The patient, aged 36, was a man from Porto Rico. There was no history of any similar condition or tuberculosis in the family. He gave no history of a previous illness bearing on the condition presented, and denied any venereal history. He stated that his occupation was that of a fireman, and that he had previously worked in Porto Rico as a laborer in the sugar and tobacco fields.

The condition began on the left foot twenty-five years ago as a small verrucous lesion about the size of a small pea. The lesions gradually became larger and more numerous, some of them running together. After five months other lesions appeared on the right foot. The lesions on the hands followed scratching of the lesions on the feet—as the patient remarked, after getting blood on the fingers from the feet. He had received no treatment. The lesions were on the hands and legs, on the dorsa of the feet and on the penis, as well as a few on the trunk. They were dark brown and verrucous in type. The greater part were discrete, but they had become confluent over the dorsa of the feet.

DISCUSSION

DR. HERMAN GOODMAN said he had seen the patient at the meeting of the Clinical Society of the New York Skin and Cancer Hospital, and he agreed with Dr. Trimble that it was ordinary verruca. Among 12,000 drafted men in Porto Rico, he had seen at least thirty cases as extensive as this one. The coffee plantations on which the patient had worked are all moist, and the men and women work barefooted. They are constantly in contact with the moist ground and get these hypertrophic warts on the lower extremities.

LUPUS ERYTHEMATOSUS CIRCINATUS OR SARCOID? Presented by DR. SCHEER.

William O'D., 27 years of age, a native of the United States, an engineer, presented himself at Dr. Fordyce's clinic on October 4 with a lesion on the left cheek of two months' duration. It began as a "pimple," which enlarged after picking so that when presented it was the size of a twenty-five cent piece. The center of the lesion was flat, the follicular openings slightly gaping. The skin was of a violaceous red color, with a raised infiltrated border topped with thick scales which when raised revealed small depressions. The scales showed many small projections, which fitted into these depressions. Histologically the section resembled sarcoid.

FOLLICULITIS DECALVANS. Presented by DR. HOWARD FOX.

W. L., a man, 30 years of age, born in Russia, a carpenter by trade, had lived in the United States for the past ten years. The disease appeared suddenly and without apparent cause about four months ago, attaining its maxi-

mum development within a week. He had never before had any disease of the scalp as far as he was aware. No members of his family were similarly affected. The eruption did not cause any subjective symptoms.

On examination, the greater part of the vertex was found to be covered by closely crowded, circular, discrete, completely bald patches averaging from one-quarter to one-third inch in diameter. These presented slight redness and numerous fine nutmeg-like pin point follicular keratoses. On palpation of the scalp, great inequalities of the surface were detected, consisting of ridges and depressions. There were no crusts or stiff hairs of favus, and a microscopic examination of the hairs showed no fungus. There was also an absence of the redness and scaling of lupus erythematosus, and there were no cutaneous lesions except those on the scalp. The patient was being treated with the quartz lamp.

PARAPSORIASIS LICHENOIDES. Presented by DR. WISE.

N. A., a boy of 12, born in Poland, and under the care of the Vanderbilt clinic, had had the disease for six months. The patient presented a generalized maculopapular eruption, the lesions varying in size from that of a large pinhead to that of a pea. Some were pale, others pink, and others red. There was no itching. Many of the lesions were slightly indurated, especially those on the neck. Treatment had been of no avail, the lesions persisting despite the use of chrysarobin ointments.

ONYCHOMYCOSIS (FIVE CASES). Presented by DR. HOWARD FOX.

These cases, from Ellis Island, were shown through the courtesy of Dr. J. W. Kerr of the U. S. Public Health Service. All of the patients were immigrants from Europe, who had arrived in the United States during the past month. They showed various dystrophic changes in the nails of fingers and toes, clinically characteristic of onychomycosis, and confirmed by microscopic examination. In each case the diagnosis was trichophytosis of the nails, though this was not culturally differentiated from favus. The individual records were:

S. G., a man 27 years of age, born in Poland, gave a history of having had the nail condition for four years. No member of his family had been similarly affected. The disease was confined to the middle finger of the right hand and ring and little finger of the left hand. The toe nails were not involved.

A. T., a woman 55 years of age, a native of Poland, stated that the nails had been diseased for thirty years. None of her family were similarly affected. She had never been treated. Four fingers of the left hand showed the presence of onychomycosis.

B. L., a woman 64 years of age, born in Poland, gave a history of having had diseased nails for about thirty years. No member of her family had had a similar disease. All the nails of the right foot, four of the left foot and all the nails of the left hand were affected.

A. G., a man 38 years of age, born in Portugal, stated that the disease had first appeared fourteen years ago. None of his family or friends had been similarly affected. The nails of the fingers and toes were diseased.

N. R., a man 30 years old, born in Italy, gave a history of nail disease since childhood. He had two brothers who had a similar condition. He had served for six years in the Italian army. All the fingers of the right hand, except the index finger, were involved.

DISCUSSION

DR. J. W. KERR, chief medical officer at Ellis Island, said that at Ellis Island a careful watch was kept for favus of the scalp and nails and many cases had been found, especially in recent months. Dr. Fox, on visiting the island in his official capacity occasionally, had been greatly interested in this class of cases and had asked that these patients be shown tonight. The diseases among aliens which were of interest to the dermatologist were grouped under what was called Class A (11), generally known as loathsome contagious diseases, including syphilis and other venereal infections, yaws and other mycotic infections. The medical inspectors were constantly on the lookout for them on account of their chronicity and importance to the public health. Favus is an exceedingly difficult disease to treat by any method, and the patients under treatment usually remain under their care from three to six months. After treatment by the roentgen ray, it is necessary to hold the patient for several weeks after the hair grows out in order to determine whether the causative organism is present, since that is the only criterion by which cure can be determined.

It was gratifying to have the members of the Section observe these cases of favus and ringworm of the nails, loathsome contagious diseases which were rather readily curable. It had been found that on removal of the nail and treatment of the nail bed the infection can be eradicated. This was different from the experience with disease of the scalp. It was the general experience that patients with favus of the nails were not likely to have favus of the scalp. This had proved to be an interesting observation to him, but one well known to dermatologists with experience.

EPITHELIOMA OF THE PENIS. Presented by DR. L. SPIEGEL.

L. J., an Austrian and a machinist by occupation, an unmarried man under treatment at the Lenox Hill Hospital and Dispensary, presented a sore on the penis of about five weeks' duration. He gave a history of a chancre fourteen years ago for which he received no treatment. He denied any sexual exposure during the last eight years. The lesion was irregular and crater-like in character, situated on the dorsum of the penis at the junction of the inner surface of the prepuce and corona glandis. It was about 2.5 cm. in diameter, the edges being hard and pearly, the base red and granular in appearance. There was a profuse serous discharge. There was no glandular enlargement. The Wassermann reaction was + + + +; there were two antigens.

Microscopic examination of the biopsy specimen showed a neoplasm consisting of strands and alveoli of stratified squamous epithelioma in which pearl formation was extensive and mitotic figures rather common. This epithelial new growth was invading the connective tissue surrounding the neoplasm in all directions. Three intravenous injections of the arseno-benzol brand of arsphenamin—a dose of 0.5 gm. each on September 26, 28 and 30—caused no improvement of the ulceration.

ACQUIRED FACIAL PIGMENTATION, WITH PROBABLE POLY-GLANDULAR TROUBLE. Presented by DR. WISE for DR. THORNLEY.

E. W., a young man 18½ years of age, under treatment at the Vanderbilt clinic, had had the condition two months; it was said to have followed sunburn. He presented an irregular mottled chloasma-like pigmentation of

the face, backs of the hands and in the axillary folds. He also presented gray hairs in the scalp and pubes, effeminate hair distribution and wide spacing of the perineum.

DISCUSSION

DR. WISE said that the case was interesting from the standpoint of endocrine disturbance. The patient had been seen by Dr. Casamajor, who suggested suprarenal and dyspituitary trouble, but nothing definite. It was interesting that a young man of 18 should have a suddenly acquired pigmentation of the face which was not chloasma. The feminine distribution of the pubic hair and the graying of the scalp hair made the case interesting from the point of view of the ductless glands.

DR. LEVIN said that the pigmentation was dependent on the endocrines. Besides the points mentioned, the patient had long extremities, long fingers with broad distal phalanges, large ears, prominent malar eminences, overgrowth of the eyebrows with a meeting of the hairs over the nose, a low downgrowth of the scalp hair on the temporal regions and forehead and a separation of the incisors.

A radiograph of the skull might show a large pituitary gland or a crowded gland enclosed in the sella turcica with the clinoid processes approaching one another. In these conditions, the suprarenals are more or less exhausted and with the disturbance in the chromaffin system the regulation in the pigment deposits is affected and patches of abnormal pigmentation appear. This is all part of a compensatory endocrine syndrome.

In a patient seen recently at the hospital, of about the same age as the boy presented, similar signs were observed, and the blood pressure proved to be low. Addison's disease was suggested, and this diagnosis was later corroborated by internists. This patient should be studied for hypo-adrenalism and for a possible beginning Addison's disease.

DR. HIGHMAN said he hesitated to discuss disturbance of the endocrine glands, though he was willing to concede the general principle that every one is the sum total of the interplay of the various endocrines—physically, morally, and mentally—but the entire subject is still in the speculative stage, and we do not know what we mean when we apply endocrinology to dermatology. Dr. Highman had no desire to cast a slur on the subject, however. It is evident from what we know of the suprarenal gland that it has a strong effect on pigmentation, but what the pituitary gland may do in these conditions we can only conjecture, and until we have more specific knowledge, we should proceed slowly. What we have heard tonight simply amounts to saying that the man has brown spots because he has them.

LICHEN PLANUS ANNULARIS. Presented by DR. PAROUNAGIAN.

F. McD., aged 25, Irish, single, a laborer, had been in this country for the past six years. There were a few scattered lesions on the forearms. About six weeks ago the patient noticed lesions on the glans penis. These did not itch. On the buccal surface of the right cheek was an annular white lesion of lichen planus. The lesions first appeared on both legs about two years ago, and have persisted. New lesions occasionally appear on the feet and legs. These itch moderately. A Wassermann test was made on October 4, but the report had not been received. There was no history of syphilis.

CASE FOR DIAGNOSIS. Presented by DR. PAROUNAGIAN.

Louis T., aged 25, a Cuban negro, married, a cigarmaker, two years ago had had gonorrhea, and treatment was administered by injections. He complained of itching and burning near the anterior end of the penis. A physician had cauterized a urethral abscess, which resulted in a fistula back of the meatus. Another doctor was then consulted; he gave three injections into the arm vein. Following this, the patient developed severe edema of the penis and inability to urinate. No Wassermann test was made. A third physician who opened the urethra to allow urination, split open the anterior portion of the urethra. The patient stated that the wound healed but never closed properly. About three weeks ago itching developed, first on the back. One week later, an eruption appeared all over the body. The patient then took some "blood pills" for about a week. At Lenox Hill Hospital he was given a brownish ointment which relieved the itching but did not influence the eruption. He had had no local applications for the past four days.

The patient could not speak English well. A tentative diagnosis of pityriasis rosea was made, and further suggestions were requested. Dr. Parounagian said he would endeavor to watch the case and report on it at the next meeting, but there were a great many more lesions on the face than when Dr. Fox saw it first, and the entire extremities were involved.

DISCUSSION

DR. HOWARD FOX thought the case unquestionably one of pityriasis rosea. The diagnosis seemed clear from the duration (three weeks) and the presence of generalized superficial, dry, scaly, discrete patches with a circinate tendency. The presence of lesions on the neck or face did not rule out pityriasis rosea.

ARSPHENAMIN DERMATITIS. Presented by DR. PAROUNAGIAN.

J. H., an Englishman, 40 years of age and single, who presented himself for treatment at Bellevue clinic, sixteen years ago had had a chancre, for which he received treatment by mouth for two and a half years. About three months ago a Wassermann reaction of + was obtained by the board of health laboratory. He therefore received ten injections of arsphenamin and sixteen mercurial injections at the Post-Graduate Hospital. Following the eighth injection of arsphenamin, he began to suffer from intense itching, erythema and a "goose-flesh" appearance of the skin. There was no weeping or moisture of the skin. About three weeks after the appearance of the generalized rash, his skin began to peel. For the past week he has had numerous pustules. The Wassermann reaction at Bellevue was + on Sept. 22, 1920.

RETARDED ROSEOLA. Presented by DR. PAROUNAGIAN.

C. M. J., from Dr. Parounagian's clinic at Bellevue, aged 35 and single, was born in the United States, a ship's storekeeper, had had an exposure nine months ago, and a chancre developed on the foreskin three weeks later. Circumcision was performed one week after the appearance of the sore. He had received one injection of arsphenamin and mercury pills for a few days. He had had no further trouble until two months ago, when a rash appeared on the cheeks and forehead. It disappeared in about two weeks.

A month ago he developed a rash on the trunk, arms and thighs. For the past three days this has been marked, especially on the arms. There was

no itching. The right tonsil showed small mucous patches; the left tonsil showed folliculitis. There was some general congestion of the throat. The inguinal glands were enlarged, discrete, shotty, but not painful. The epitrochlears were negative; the anterior and posterior cervical glands were moderately enlarged. The Wassermann reaction, Sept. 28, 1920, was + + +.

LICHEN NITIDUS. Presented by DR. PAROUNAGIAN.

Z. M., a Greek, 19 years of age and single, a bus boy, first noticed the lesions about a year ago. He stated that for the past year he had lost weight, although he felt well and strong. He had never had a severe illness, and he denied venereal disease.

The lesion consisted of minute shining papules, mostly follicular in character, more pronounced on the flexor surfaces and most noticeable on the chest, back and genitals. There had never been any itching. The dorsum of the tongue showed whitish plaques of a membrane-like appearance. The lesions on the glans penis were annular, with a good deal of scaling and some pigmentation. The scrotum was studded with shining, irregular papules, closely resembling lichen planus. The Wassermann reaction was negative on Sept. 28, 1920.

DISCUSSION

DR. WISE said that the lesions on the shaft of the penis and back of the neck were characteristic of the disease as described in the textbooks, and were similar to those demonstrated by Dr. Trimble last year; but he was puzzled by the large papular lesions on the glans penis. If one saw only the glans penis he would think it was lichen planus, but the combination of the two was unusual. There was no relationship between the two, and any diagnosis should be corroborated by microscopic examination of the lesions on the back of the neck and on the glans.

DR. LANE said that the lesion on the penis covered the whole glans and was not limited to the site of the circumcision scar. He did not remember whether lichen nitidus had been described as affecting the glans. When he first saw this lesion he had considered it lupus erythematosus, but on closer examination he had considered it lichen planus. He agreed with the diagnosis of lichen nitidus on the shaft of the penis.

DR. WISE said that the lesions on the glans penis were almost the size of a lentil, altogether different from the pinhead lesions on the shaft. The lesions appeared to him like two entirely different conditions.

DR. PAROUNAGIAN said that when he first saw the case he had remarked that the lesions on the penis looked like lichen planus, but after considering all the symptoms together, he had decided it was not that.

PHAGEDENA OF PENIS: MIXED INFECTION. Presented by DR. PAROUNAGIAN.

M. W., a seaman, aged 22 and single, born in the British West Indies, had had a chancre at the sulcus eight and a half months ago. Later he developed a balanitis and a circumcision was performed three months after the appearance of the chancre, but the wound never healed. The phagedenic ulceration destroyed a large part of the skin of the penis, and ulceration of the corpus spongiosum produced a loss of a large part of the anterior urethra.

At Kings County Hospital on July 27, the Wassermann reaction was + + + +. He was given six arsphenamin and five mercury injections. At the end of this treatment the Wassermann reaction was +, but the genital ulceration remained unimproved.

He appeared at the Bellevue clinic on September 22. The Wassermann reactions on September 22 and 28 were both negative. A Ducrey examination made on September 24 was positive. He had received arsphenamin on September 23, 27, 30 and on October 4. On September 30 and October 4 the ulcerated area was irrigated with arsphenamin solution, 0.1 gm.; this was followed by slight improvement. Suggestions as to treatment were requested.

DISCUSSION

DR. TRIMBLE asked whether the man had syphilis also.

DR. PAROUNAGIAN replied in the affirmative; but the man had had the chancre eight and a half months ago.

LICHEN PLANUS NODULARIS. Presented by DR. SCHEER.

Mrs. S. E., from the Vanderbilt clinic, aged 52 years, had lesions located on both legs, and there was one patch on the left elbow. There were numerous nodular discoid elevated, reddened and indurated lesions scattered over the legs and knees, associated with itching. The patient had had eleven roentgen-ray treatments, $\frac{1}{4}$ units (skin distance) once a week, resulting in great improvement. Previous treatment had not been beneficial. The mucous membranes were free. The Wassermann reaction was negative.

POSTARSPHENAMIN PIGMENTATION: ARSENICAL KERATOSIS.

Presented by DR. HERMAN GOODMAN.

A man, aged 32, had had a chancre on March 1, 1920, followed by an adenopathy of the groins and a general eruption in April. The Wassermann reaction was + + + +. Arsphenamin treatment was instituted during the secondary stage of the disease. The patient received twenty-two injections, receiving injections twice a week. Treatment was then interrupted because the eruption appeared; it was renewed until a total of thirty injections had been given. No mercury injections had been given. The patient received drops and rubbings. It had not been practicable to get into communication with the doctor who treated the patient to learn the dosage and preparation used. The patient was seen for the first time the previous night at the West Side Dispensary (service of Dr. Leo Michel). He had previously made one visit to the Post-Graduate Dispensary in New York.

DISCUSSION

DR. HIGHMAN said that he had had an opportunity to examine the patient by daylight at the Post-Graduate Hospital, and he very much doubted the history of syphilis. He was told that the patient's Wassermann reaction was positive, and that he had received arsphenamin, but the pigmentation seen last week suggested the pigmentation left by lichen planus. At that time also the patient said the eruption itched. Whether or not he had had syphilis, the remaining pigmentation was quite characteristic and was much more likely to be that of a faded lichen planus than the result of arsenic.

DR. LAPOWSKY inquired concerning the kind of lesions on the lower extremities.

DR. HIGHMAN replied that they were just such simple small brown pigmentations or spots as were seen after lichen planus—precisely as shown tonight.

DR. WISE inquired whether it would be possible to get an arsenic reaction from a piece of tissue. Had any one obtained arsenic from the tissue in such a case?

DR. HIGHMAN replied that Unna had described an arsenic reaction, but that he himself had not been able to make it work.

DR. GOODMAN said that the absence of lesions on the mucous membranes influenced him against accepting a diagnosis of pigmentation following lichen planus. He believed that the pigmentation was on the site of the secondary syphilitic eruption. The keratoses present about the waist, where there was irritation from the wearing of a belt, led him to believe it to be the result of arsenic. Should the patient permit, a section would be taken for further study.¹

FOLLICULITIS CHRONICA ATROPHICANS. Presented by DR. ABRAMOWITZ.

Lena W., aged 22, a Russian Jewess, was referred to Dr. Fordyce's clinic by Dr. Thornley of Gouverneur Dispensary. The eruption was of about five years' duration and was located on the chest, back, back of the thighs and extensor aspect of the extremities. It consisted of many fine comedo-like plugs, with depressed scars about the size of a pinhead and smaller. These were scattered diffusely over the above areas, with an occasional follicular pustule here and there.

DISCUSSION

DR. WISE said he had seen the patient for the first time during the evening. Dr. Trimble had suggested the diagnosis of acne keratosis, a name given by Crocker to a condition characterized by blackheads and subsequent atrophy. He himself had never before seen a case of this kind.

DR. TRIMBLE expressed the opinion that the case would come under the classification he had mentioned. Crocker had reported two or three cases and called them acne keratosa. In Crocker's cases the lesions were located on the face and shoulders. He, himself, had seen another case in which the arms and face were involved. The malady was something like acnitis, the only difference being that there were little horny spines which eventually fell out, leaving punctate atrophy as in this case. The lesions in this instance were more numerous than in the case he had seen, but he was convinced that it was acne keratosa, described by Crocker.

DR. ROSEN said that he had examined the case carefully at the clinic. He had never before seen a case of the same type. The active lesions looked like the lesions of a lichen scrofulosorum. A few of the lesions on the upper extremities were possibly acnitis. The microscopic picture would probably reveal some form of tuberculid of the skin.

TUBERCULOUS GUMMAS. Presented by DR. LEVIN.

M. R., a married woman, aged 45, was born in this country and had always been well. Her family and past history were negative. The condition began about fifteen months ago with a swelling of the left leg. The swelling was

1. The patient was seen the next night. He brought a report of a negative Wassermann reaction from the Post-Graduate Hospital. He was leaving for another city within twenty-four hours.

painful, softened slowly, and formed an ulcer at the end of two months. New swellings gradually appeared over the lower extremities and back, which also tended to ulceration and healed slowly. When the patient first came under observation, two months ago, there were about a dozen large pea-sized to cherry-sized hard and soft growths scattered over both lower extremities. The skin over the lesions was normal and purplish in color. An unhealthy quarter-dollar sized ulcer with undermined purplish edges was present on the front of the left leg. Under observation, the new hard nodules grew slowly to involve the skin, softened and ulcerated. Scattered over both lower extremities were numerous hard and soft subcutaneous nodules which showed a tendency to become confluent and form soft matted-together masses. The skin over these nodes was purplish red in color. On the left leg and on the outer aspect of the right thigh were half-dollar sized, irregular unhealthy ulcers with granulating floors and undermined edges. The discharge from these ulcers was purulent.

Pathology: Tuberculosis. The Wassermann reaction was negative.

LEUKODERMA PSÖRIATICUM. Presented by DR. ABRAMOWITZ.

Mary B., 10 years of age, born in the United States, was brought to the Vanderbilt clinic with extensive macular leukodermatous patches on the forehead, trunk and extremities, and with typical psoriatic patches present on different parts of the body. There was no definite history of using chrysarobin nor any signs of chrysarobin dermatitis. The patient had been using white and black salves, but denied that they stained her clothes.

EPIDERMOLYSIS BULLOSA ACQUISITA. Presented by DR. WISE.

Mrs. G. C., aged 21, exhibited a condition with which she had been suffering for eight months. She presented evidences of healed vesicles and bullae on the bends of the elbows, the hands, face and feet. The middle finger of the right hand, ulnar side, presented an active vesicle due to pressure from the adjoining ring. The skin of the elbow region showed moderate atrophy. There were epidermal cysts on the fingers and on the shells of the ears. The lesions arose both spontaneously and as a result of traumatism.

The term *acquisita* was included in the title of the case because the patient was the first member of the family to show the conditions.

DISCUSSION

DR. LAPOWSKY said that "*acquisita*" meant acquired, not hereditary. If the term acquired were introduced in epidermolysis bullosa, it could only mean that the patient was the first in the family who acquired the epidermolysis bullosa. In expressing such a condition it would be better to use a more descriptive form, as "first in the family," and not the word "*acquisita*."

DR. ABRAMOWITZ said that the patient was positive that she had never had the condition before nor had any member of the family or relatives had the disease, and that this disease occurred after a normal confinement. She had had lesions on the nose and in the mouth, and some on the body, which seemed to have cleared up under arsenic which she had been receiving. She had never noticed that her skin was vulnerable in any way, particularly to injuries that produced blebs or bullae. She said that sensitiveness was acquired since she had had the first attack of bullous eruption after her confinement. There was no consanguineous marriage.

DR. WISE said that Dr. Lapowski's point was well taken, but that name had been used long before by others. It was applied to cases in which the family history for generations back was obtained and was negative. Why the patient should have lived for twenty-one years without any previous manifestation of the condition was a question.

LUPUS ERYTHEMATOSUS DISSEMINATUS. Presented by DR. BECHET.

B. H., a female adult from the service of Dr. Trimble at the University and Bellevue clinic, stated that the eruption had been present for thirteen months. It began on the nose and soon thereafter appeared on the cheeks. In July, 1920, the fingers and backs of the hands became involved. A few weeks later the eruption appeared on the chest, neck and arms. These lesions consisted of various sized plaques with symmetrical spots on the extensor surfaces of the third phalanges of the fingers. They were sharply margined, of a rather dusky red color and slightly scaly. There was congestion and slight atrophy at certain points apparently undergoing involution. Burning and itching, so frequently complained of in this type of lupus erythematosus, was also present. The patient appeared to be in good health. A physical examination proved negative. The patient's mother, four brothers and one sister had always been well. Her father had died of gastric carcinoma several years before.

DR. BECHET said that the lesions were quite large, one of them on the back of one hand being almost 2 inches in diameter. He had observed them for two months, and in that time there had been no change in their appearance. There were no papules or vesico-bullae. The plaques were dry, slightly scaly, and in a good light were atrophic in the center. The face was greatly involved. In view of these facts a diagnosis of disseminate lupus erythematosus seemed more obvious than erythema multiforme.

CARCINOMA OF TONGUE. Presented by DR. PAROUNAGIAN.

T. D., a man of 51, born in the United States, a bartender, gave a history of chancre a year ago, which received only local treatment. He entered the Bellevue clinic on Aug. 2, 1920, with a history of ulceration of the tongue of four months' duration, which was gradually increasing in size. Examination showed an irregular ulcer on the left side of the dorsum of the tongue, about 2 inches from the tip. Another isolated area was present on the left lateral aspect of the tongue, anterior to the first one. The anterior cervical glands on the left side were enlarged. The Wassermann reaction on August 2 was + + +. The treatment consisted of arsphenamin, 0.15 gm., administered on August 5, 12, 16, 19 and on September 9, 16 and 23.

On August 31 the patient was referred to the General Memorial Hospital for radium treatment. It was not thought wise to use radium. On September 7, Dr. Douglas in consultation advised against operation.

The patient was having increasing pains in the tongue and for the last few weeks had complained of pain in the throat and difficulty in swallowing.

DERMATITIS HERPETIFORMIS (PAPULAR FORM). Presented by DR. WISE.

Louis S., a Russian Jewish pedler, 52 years of age, applied at the Vanderbilt clinic for treatment of a skin trouble of seven years' duration. The trouble disappeared during the winter and spring but recurred during the summer.

The eruption consisted of pruriginous papules—some of them excoriated—located on the extensor surfaces of the extremities and on the back of the shoulders.

PRECANCEROUS DERMATOSIS? XERODERMA PIGMENTOSUM?

Presented by DR. L. CHARGIN.

A woman, aged 35, an Italian, married and the mother of four children, since early childhood had been affected with freckle-like spots which were located especially on the upper chest, arms and face. The lesions increased



Precancerous dermatosis.

in size and in number, in the course of years, making their appearance on the back, abdomen and legs and becoming especially thick on the neck and face.

At the time of presentation, the face, neck, upper chest and arms were greatly affected; while the back, abdomen and legs showed numerous but scattered lesions. The lesions consisted of freckle-like spots—most of them with a slightly raised and verrucous border—small atrophic areas with similar borders, crusted and fungoid tumor masses and cutaneous horns. The flat lesions were for the most part yellowish or brownish in the center with darker pigmented borders; many of them, however, were distinctly red. Most of the

verrucous lesions were darkly pigmented. The tumor formations were red and irregular over the surface as well as in outline. Scraping the flat lesions, a pellicle was easily removed, revealing a moist red, slightly oozing surface. The lesions varied in size from that of a pinhead to that of a twenty-five cent piece; they were for the most part in close apposition, and in many areas were confluent. The tumor formation varied in size from that of a pinhead to $2\frac{1}{2}$ inches in their longer diameter.

The tendency to epitheliomatous degeneration began about three years ago, and at the time of presentation there were about a dozen lesions. Under the right eyelid and on the back of the right hand were cutaneous horns.

The patient complained of no subjective symptoms, and her general health was good. The urine and blood Wassermann tests were negative. None of her offspring was similarly affected, but a brother of the patient was said to be suffering from a mild type of the affection.

Dr. Chargin said that though the patient presented many of the characteristics of xeroderma pigmentosum, there was absence of others, such as the telangiectasia, the general thinning or parchment-like skin. After making a biopsy, Dr. Highman reported precancerous dermatosis.

MORPHEA. Presented by DR. ROSEN.

Elizabeth F., aged 37, presented a patch of morphea on the left flank in the waist line, roughly triangular in outline and about 6 inches long, the base being about 3 inches. The patch was pink in color and was slightly indurated. There were three smaller patches on the right side of the abdomen.

CHICAGO DERMATOLOGICAL SOCIETY

Regular Meeting, Oct. 20, 1920

C. A. BAER, M.D., *Presiding*

ARSENICAL HYPERKERATOSES. Presented by DR. H. N. COLE.

A man, aged 22 years, with a history of epilepsy of nine or ten years' duration, four years ago had first noticed papular lesions on the palms and soles that were becoming keratosed. At that time he was told that arsenic had not been used, and that he had been given only sodium bromid.

Two or three of the lesions had been treated experimentally with radium, which caused temporary disappearance. The patient then consulted another physician who administered roentgen therapy; he subsequently returned to Dr. Cole with a more acute case of keratosis. He had received no arsenic since first seen but had formerly received arsenic with sodium bromid over a long period of time. Hyperpigmentation was present under the arms.

ARSENICAL HYPERKERATOSIS AND PIGMENTATION. Presented by DR. WAUGH.

A boy, aged 9 years, had received Fowler's solution for chorea two years previously, beginning with a dose of 5 minims after meals which was gradually increased to 10 minims. Three or four months later the patient's mother noticed a roughness of the palms which later spread to the dorsal surface of both hands and fingers. The plantar surfaces were similarly involved.

Examination revealed small, hard, scaling, hyperkeratotic lesions, so numerous as to be indistinguishable over most of the palmar surface, but on the dorsal surface the individual lesions were quite distinct. There was generalized dusky brownish pigmentation of the skin, which was most marked over the chest, back and abdomen.

DISCUSSION

DR. COLE thought the interesting fact was that most of the process had formed after arsenic administration had been discontinued.

DR. ORMSBY thought it was interesting to see patients of this sort because it was hard to explain why the condition often progressed after the drug was discontinued. When arsenical keratoses were started they frequently continued for years after discontinuance of the drug. The pigmentation and other symptoms would largely disappear, but the keratoses would remain. Arsenic seemed to originate some process in the patient which persisted in spite of removal of the exciting factor.

DR. FOERSTER stated that he had recently seen two cases in which epithelioma developed on arsenical keratoses. In one of the cases arsenic in small doses had been taken for a long time to prevent a bromid eruption, the bromid being given to control epileptic attacks. The growth developed on one finger. The other patient developed an epithelioma on the foot after having taken arsenic for a long time for psoriasis.

DR. PUSEY said that twenty years ago he had made a photograph of arsenical hands, when this condition was not as commonly recognized as it is now. Fifteen or sixteen years later the man returned with epithelioma and subsequently died of carcinoma. He agreed with what had been stated about the persistence of arsenical keratosis after the drug was discontinued, but he had had an interesting experience in that connection. A man with this disorder well developed on the palms and a history of having taken arsenic had been told by him that the trouble was permanent. The patient then consulted one of his colleagues and the growths disappeared; hence, it was not certain that early arsenical keratosis always persisted or became worse.

DR. BARR thought the methods by which patients secured arsenic were rather interesting. In a case of arsenical neuritis seen by him the patient was in the habit of chewing match sticks. This was the only arsenic he received, but laboratory tests showed it to be present in the match sticks.

CASE FOR DIAGNOSIS. Presented by DR. WAUGH.

The patient was the child who was shown at the May, 1920, meeting of the Society, with the history of having at birth an unusual amount of coating over the body, which dried and resembled a collodion covering; it began to exfoliate in large sheets at the end of forty-four hours.

Subsequent History: The child had nursed normally, gained in weight and slept normally, but the skin had exfoliated four or five times. Following the exfoliation the surface appeared perfectly normal in some places, but there was an ichthyotic appearance in others. Soothing ointments and bland lotions had been used.

DISCUSSION

DR. ORMSBY said that he had made a suggestion before in this case and thought it still held. The cases were formerly described as ichthyosis; Bowen first called attention to the fact that they were different from ichthyotic cases.

Immediately after birth the skin looked as if it were covered with collodion, and it was smooth and shiny. Subsequently some infants developed ichthyosis but many of them died; the patient he had shown several years ago lived only three weeks. Bowen thought the condition was due primarily to a retention of the epitrichial layer, which was not thrown off at the time it ordinarily should have been during gestation. The point of interest was that the cases were so closely allied to ichthyosis but were not identical.

DR. FOERSTER asked whether the child had been given thyroid preparation.

DR. WAUGH stated that the child had received only local treatment. The interesting point to him was the length of time the baby had lived. In 1895 Bowen reported five cases of this disorder, and in 1909 others were recorded by the same author, but few of the patients had lived more than a few weeks. This child was now a little more than 5 months old, and, as far as the skin element was concerned, it would probably live indefinitely.

A CASE FOR DIAGNOSIS. Presented by DR. FINNERUD for DR. ORMSBY.

A colored man, aged 29 years, presented areas of hyperpigmentation of one year's duration, situated chiefly on the forehead, temples and cheeks, but also present on the upper chest in front and behind. The macules were of irregular outline and fairly sharply demarcated; they were from grayish-blue to purplish, and in all instances darker than the surrounding grossly normal skin. The lesions varied in diameter from the size of a pinhead to that of a silver quarter or more, the only large areas being on the forehead near the scalp hair line; most of those of the chest and cheeks were chiefly the size of a match-head or smaller. There had never been any swelling or subjective sensation. The patient had always been in good health and denied all venereal, drug and previous skin history, except a possible Neisserian infection, for which he received no silver salts.

DISCUSSION

DR. FINNERUD could suggest no diagnosis. There was no history of the use of drugs, and he did not know whether there was any preceding inflammatory condition; according to the patient, there was not. The patient sought relief because he considered the spots disfiguring.

DR. GUY said that the man admitted a urethritis in 1918, and said that he took pills for two weeks at that time. He thought that, on account of the peculiar bluish color of the spots with mucous membrane involvement and the absence of any preceding inflammatory process, it might be an argyria.

DR. ORMSBY said that he saw the patient for the first time in the clinic the day before and obtained no record of his use of argyrol or other silver preparations. The patient said it was embarrassing to have the black spots.

LICHEN PLANUS SCLEROSIS ET ATROPHICUS. Presented by DRs. ORMSBY and MITCHELL.

A woman, aged 59 years, had had the disorder for one year. The lesions were typical, flat, white papules, situated chiefly on the front of the neck and over the clavicles. The papules presented hyperkeratotic horny spines typical of the disorder. In addition, there was some atrophy where the papules had undergone involution. There were no subjective symptoms.

The patient was receiving roentgen therapy, a method which had proved successful in similar cases.

DISCUSSION

DR. ORMSBY considered this a typical case of lichen planus sclerosis et atrophicus, and he had presented it merely as an example of that disease. The patient had first been seen two months before.

DR. COLE said he had a case of lichen planus atrophicus with typical lesions on the clavicles under observation. On the back there were two lesions about half the size of the palm, with the whole area hypertrophic. Over these areas there were some atrophic spots with a plug in the center, while around the abdomen was a characteristic band of the same sort.

DR. SENEAR was reminded by Dr. Cole's case of the one he had presented last year with Dr. Pusey. The patient was a woman with numerous discrete and grouped lesions with a single large patch. In diagnosis it was difficult to make a differentiation between white spot disease and lichen planus atrophicus, but he had felt that it was the latter condition. In the case now shown, Dr. Ormsby had called his attention to certain differences, and he was now inclined to think their case was one of white spot disease. He had recently seen another case similar to the one shown last year, but with more eruption and without the plaque present in their other case and in the one now mentioned by Dr. Cole. He believed that Dr. Ormsby's case was a lichen sclerosis, but in the other two cases there was more doubt as to white spot disease.

LUPUS ERYTHEMATOSUS. Presented by DR. LIEBERTHAL.

The patient was a woman, aged 24 years, whose trouble started a little over a year ago with spots on the left cheek, which gradually developed also over the forehead, right cheek and nose.

The spots were red, slightly raised on the periphery, more or less rounded, with desquamation. No subjective symptoms had been noted at any time. Most of the lesions had healed, but traces remained of some of them, and there was a typical lesion in the right zygomatic region, slightly thinned out. Her general condition was good.

DISCUSSION

DR. LIEBERTHAL said he had learned to be exceedingly careful about using powerful treatment in these cases. In the superficial form of the disease, as in this case, he believed the mildest treatment was necessary. During the last six months he had treated several patients with a simple application that had been recommended twenty-six or twenty-seven years ago by H. von Hebra, and which consisted of rectified alcohol, ether and peppermint water, equal parts. This was painted over the affected areas every two or three hours and had given good results in every case, whereas severe treatment did not give good results in the superficial form.

DR. PUSEY asked whether any one had obtained good results from painting the chronic patches of lupus erythematosus with phenol. He had recently seen a case in which an excellent man had used liquid phenol with great improvement.

DR. McEWEN asked whether any one had found lupus erythematosus associated with streptococcus infection, as reported in recent issues of the *British Journal of Dermatology*. He thought focal infection should be considered a possible cause in this case.

DR. PUSEY said he had recently seen an acute lupus on the face with a sinus infection. His attention was first called to the bland treatment by Crocker.

DR. OLIVER said he had seen seven cases of lupus erythematosus at Rush Dispensary last year and they had all seemed to improve a good deal on quinin, 2 grains, three times a day, with a simple zinc oxid and calamin lotion.

DR. FISCHKIN said that lupus erythematosus is so uncertain as to the results of treatment and is comparatively so frequent that one is compelled to try all kinds of treatment. After the mildest remedies have been used without any results, one is inclined to resort to stronger methods of treatment. He had used all methods, among them, Hollander's quinin and iodine, carbon dioxid, ultraviolet and roentgen rays; in some cases he had secured good results with the latter when all other methods had failed.

DR. LIEBERTHAL emphasized the fact that he used the bland treatment in only the superficial cases. In severe cases he used carbon dioxid but did not apply it for longer than five seconds for each treatment. In chronic cases with deep lesions, he agreed with Dr. Fischkin that the ultraviolet ray sometimes worked like a charm, but this was not true in all cases.

DR. ZEISLER recalled two cases that had been cured with tuberculin that had failed to respond to other treatment. The doses of tuberculin were small, and improvement might have been merely a coincidence.

HYDROA. Presented by DR. WAUGH.

A colored girl, aged 10, had had the disorder seven years. There were numerous vesicles, most of them the size of a split pea, on the dorsal surface of the hands and extensor surface of the forearms; over these areas there were also many scars from former lesions. A similar condition was present on the legs below the knees. The skin on the neck and lobes of the ears was rough, scaling and thickened; scarring in these areas was not pronounced. The eruption was associated with marked pruritus. It disappears entirely during the winter, recurring in the spring.

DISCUSSION

DR. PUSEY had thought of hydroa, but there were some lesions in the palms, where the exposure to light was slight, and he thought the case would not fit in with a hydroa estivale. He thought it was a lichen urticatus (a papular eczema) on the extremities, with some vesicle formation.

DR. WAUGH considered the case interesting on account of the rarity of the disorder and the fact that the arms and legs were so extensively involved. To him the recurrent and small eruption was also of interest. He had seen a woman several months ago who had had a recurrent eruption about the neck for five years, where the skin was uncovered, and on each arm above the elbow where the skin was covered with the sleeves. If she remained out of the sun it would disappear but if she were outdoors, even though the skin was covered, it would reappear. No vesicles were present at any time, but there was itching similar to that present in the case shown. There was no eruption on any other part of the body. He wished to know whether anything could be done to prevent a recurrence in this group of cases.

DR. SENEAR had nothing to suggest as to therapy, as he was unable to make a definite diagnosis. The case impressed him as belonging in the lichen urticatus group rather than in the hydroa estivale group. No dermatographia was present, but there was a distinct urticarial element. He had seen only two cases of true hydroa and in both of those the scarring was deep and characteristic, while in this case it was not definite.

A CASE FOR DIAGNOSIS. Presented by DRs. ORMSBY and MITCHELL.

A man, aged 26 years, presented a disorder which had been present for twelve years. The lesions were brown patches situated on the lower extremities, and the eruption was about equally distributed over both thighs and both legs. The size of the patches varied from that of a fingernail to that of a palm; some were larger. The chief characteristic was pigmentation, but in addition there was telangiectasia and in some areas distinct atrophy. As a whole, the patch presented a reddish-brown center and a lighter brown periphery. The patient said that there were no subjective symptoms, that the patches were slowly increasing in size and that no patch had disappeared.

DISCUSSION

DR. WILE thought no one could venture a definite diagnosis of the case because at the present stage it apparently did not fall into the category of any known disease. To him it suggested definitely that the patient was bleeding into his skin, and for that reason one would look for some change in the chemistry or physical condition of his blood. He apparently had an unusual form of purpura which persisted and spread peripherally. Dr. Wile thought it would be interesting to know something of the coagulation time of the blood, either in the patient himself or in his antecedents, as he might belong to a family of hemophiliacs. An investigation along this line might lead to a proper understanding of the pathologic physiology of the process.

DR. PUSEY said the case did not appeal to him as a disturbance in the blood but rather as a local disturbance in the blood vessels. Dr. Foerster had called his attention to the fact that there were telangiectasies in the lesions, and Dr. Pusey's impression was that it was a vascular disturbance. The situation was this: The man had permanent hemorrhagic spots, long present, which remained in the same place. It seemed to him the appearance which was suggested was rather one of some disturbance in the blood vessels in these areas which provided for extravasation, and that was the probable explanation. He thought it was not a purpura annularis telangiectodes, but an analogous process.

DR. ORMSBY stated that he had seen a similar case several years ago, the only difference being that the disease in the other patient had progressed further. When the former patient was shown, many thought the cutaneous condition was due to radiodermatitis. The patient had pigmentation, telangiectasia and atrophy in areas, but to a more pronounced degree than in this case. Even after considerable investigation a diagnosis was not made. When that patient was first seen he had an indurated lesion on the glans penis which was followed by metastatic growths in the groin, with subsequent generalized metastatic growths. At necropsy the diagnosis of lymphosarcoma was made, the opinion being that it originated in the glans. The superficial cutaneous lesions had been present for years and apparently bore no relation to the

sarcomatous condition which developed at a later date. The histology of the cutaneous lesions revealed nothing. In his opinion, the present case presented similar cutaneous lesions. No biopsy had been made in this case as yet, but one would be made and reported on later. He thought these two cases were in a class by themselves.

LYMPHANGIOMA. Presented by DR. ORMSBY.

A girl, aged 14, had a group of lesions on the eyelid and a tumor mass in the mouth occupying one half of the roof on one side, extending backward to and involving the pillar of the pharynx. They had been present since birth, but had caused trouble only during the past seven years. The lesions in the mouth occurred as a lobulated mass covered with vesicles. Some involvement of the blood vessels was probably present as parts of the mass presented a deep bluish shade. The eyelid lesions were typical of a simple lymphangioma.

DISCUSSION

DR. PUSEY thought it was an interesting case of lymphangioma, with an unusual distribution.

DR. ZEISLER asked what treatment was to be used.

DR. ORMSBY said that they would use radium as it was more convenient to use in the mouth.

TRICHOPHYTOSIS. Presented by DR. WAUGH.

A woman, aged 40, whose disorder had been present for four years, did not remember which nails were first involved. At the time of presentation most of the nails on the hands and one on the right foot presented a broken, ragged, dirty brownish appearance, with a distinct teased appearance in places. The trichophyton fungus was found microscopically.

DISCUSSION

DR. LIEBERTHAL agreed with the diagnosis of trichophytosis, and stated that the nail plate was lifted up and split horizontally, which was indicative of this disorder.

A CASE FOR DIAGNOSIS. Presented by DR. ZEISLER.

A woman, aged 47, had an eruption which had been present for four years on the body and arms. The condition was apparently stationary at the time of presentation.

The lesions were indurated plaques on the neck and back and scattered over the body. She had been seen first by Dr. Zeisler on the day before presentation. A biopsy had been made by Dr. Stillians previously who, he hoped, would report his findings. The Wassermann reaction was negative.

DISCUSSION

DR. WILE suggested the diagnosis of "erythrodermie" possibly premycotic, and thought one could say nothing more than that. It was well known that the scaly erythrodermas, so-called, or parapsoriasis, which were excessively

pruritic, might develop mycosis fungoides. The crescentic lesions on the forearm could probably be considered as more than presumptive evidence that it belonged to the premycotic form.

DR. STILLIANS said that he saw the patient last year and showed her with the idea of a premycotic eruption in mind. A biopsy had revealed nothing, and the investigation was negative.

DR. PUSEY asked whether Dr. Wile used the term erythroderma in the sense of parapsoriasis. He questioned the propriety of speaking of erythroderma in that technical sense as a possible premycotic lesion. He thought many of the patches were very much like chronic eczema; many might be taken for parapsoriasis but others could not.

DR. WILE thought there was just as much reason for saying it was a parapsoriasis as a premycotic condition. The presence of extreme pruritus, he thought, was presumptive evidence that it was a premycotic dermatosis. He asked whether it was not a fact that the Society had seen several cases presented as parapsoriasis, which subsequently developed mycosis fungoides. He thought he recalled two or three such instances.

DR. PUSEY asked whether the Society had not also seen several cases presented as the premycotic stage of mycosis fungoides, which had not developed into mycosis fungoides. The premycotic stage of mycosis fungoides had become a sort of refuge in times of perplexity; nearly every time we see a dry dermatitis we cannot make out, we are likely to talk about the premycotic stage of mycosis fungoides. He believed this woman did not have the premycotic stage. It seemed to him that many of the lesions might be those of chronic eczema in a fat, dirty person. The puzzling things were the velvety lesions in front of the axillae; they did not fit in either with parapsoriasis or the premycotic stage of mycosis fungoides.

DR. COLE thought several of the lesions showed a condition of lichen Vidal, but he was inclined to believe that it might be the premycotic stage of mycosis fungoides.

DR. ZEISLER stated that he had recently seen a case that was almost identical with this one. The man had visited the Mayo clinic, and had had his teeth and tonsils taken care of, with no improvement in the cutaneous condition. He administered Fowler's solution and roentgen therapy, and the condition cleared up entirely. The eruption had been present for four years and was intensely pruritic, and this was the first treatment that had ever helped him. Dr. Zeisler did not know what the diagnosis was, but he believed the case was parallel to the one presented.

DR. FINNERUD said the patient had been at the Rush Medical College Dispensary, where the treatment given was that for lichen simplex chronica. She had given the impression that she had lesions only on the extremities.

ICHTHYOSIS. Presented by DR. STILLIANS.

A woman, aged 40, had had ichthyosis since early childhood. There were five children in the family, all girls; the first, third and fifth had ichthyosis while the second and fourth did not have the condition. The fourth child died in infancy. The skin of the trunk and limbs was dry and slightly scaly, with the exception of the skin of the palms and soles, which was thickened and demarcated in large figures. The lower part of the face was also involved.

DISCUSSION

DR. STILLIANS wished to know whether he would be justified in giving thyroid in the case. The patient had been using glycerin on the hands.

DR. PUSEY thought it would be well to keep the patient's skin greased, and believed it would do no harm to administer thyroid extract and watch the effect. Greasing the skin was the only measure he knew that caused improvement. He was interested in the improvement in the condition of the hands.

DR. ORMSBY stated that he had found 25 per cent. glycerin and 75 per cent. olive oil effective in such conditions. This was suggested to him by Dr. Morris several years ago, and he had used it ever since with excellent results.

VON RECKLINGHAUSEN'S DISEASE. Presented by DR. ZEISLER.

The patient was a woman, aged 35 years, whose disease began in early childhood. No other members of the family were affected. The tumors were generalized over the body. The patient was presented for therapeutic suggestions.

DISCUSSION

DR. PUSEY asked whether the woman was duller than normal. He had been looking for stupid patients with von Recklinghausen's disease for a long time but had seen few that were below normal mentally.

DR. ZEISLER stated that the patient's mentality seemed to be normal.

LUPUS VULGARIS. Presented by DRs. ORMSBY and MITCHELL.

A boy, aged 14, had had the disorder for seven years. His condition was unusual in that he presented a markedly elevated nodular mass about 2 cm. in diameter, situated on the left cheek just in front of the zygoma. He had previously suffered with tuberculosis of the knee joint.

LESIONS OF THE LIPS. Presented by DR. FISCHIKIN.

A Mexican woman presented a lesion of the lips which had begun eight weeks previously. There were sores in the mouth but no lesions on the body. The lips were greatly swollen, red and crusted. There was a history of a similar attack fourteen years before.

DR. GUY stated that in his service in the army there was a case similar to this one. During the investigation they found a fusiform bacillus and a spirillum, and on local application of arsphenamin the patient recovered. The case did not agree with a Vincent's angina clinically, and he did not think the present one did.

DR. COLE thought the case was rather unusual and, as the patient was a Mexican, an unusual disease might be suggested, but some of the more common diseases should be considered as well. He had thought of impetigo with streptococcus and believed this might be the condition. The lesions on the mucous membranes were like those described by Dr. Montgomery many years ago.

DR. WILE was inclined to agree with Dr. Cole. The rapid course of the disease indicated some acute infection. It was not impossible that it had been caused by infection from her teeth or from some streptococcal infection,

not necessarily in the mouth. He recalled the case mentioned by Dr. Stokes in which the upper lip looked like the one in this case, but the lower lip was not involved. He also recalled the case of a patient with a similar upper lip, a young boy, that turned out to be glanders. It looked exactly like this, and the patient died within a short time.

Dr. ZEISLER stated that he had recently seen two cases of impetigo in brother and sister with involvement of the lip in one. He believed that if syphilis could be ruled out, impetigo should certainly be considered.

Dr. LIEBERTHAL thought that antisyphilitic treatment should be instituted, not intensively but in order to rule out syphilis, if possible.

Dr. FISCHKIN said he could not elicit much of the history, but the physician who brought the patient said the Wassermann reaction was negative. Dr. Fischkin saw the patient for the first time just before presenting her. He thought it was a pus infection and suggested appropriate treatment, an astringent wash for the mouth and a small amount of mercurial ointment for the lip to be applied for a few hours each day. If this treatment proved successful, the diagnosis could be made.

ANGIOKERATOMA. Presented by Dr. FISCHKIN.

A girl, aged 7, first seen seven weeks previously, had a congenital nevus vascularis over the lateral aspect of the left thigh, extending from below the knee to the buttock, with numerous large angiectases. There was no history or sign of chilblains. Two years ago minute, dark red, elevated lesions, whose size ranged from that of a pin point to that of a pinhead, appeared in different parts of the nevus. Some of them became the size of a pea or larger, becoming harder in time, with black, rough tops, assuming a warty appearance. They gave no inconvenience, with the exception of bleeding when scratched or bruised. Some of the lesions were red, elevated, flat tumors, dotted with black spots; others were solid, warty excrescences. Many of them Dr. Fischkin had removed by means of electrolysis, their location being marked by black crusts. There was a pinkish scar in the middle of the thigh, which was the result of chemical cauterization employed by a physician two years previously, on the edge of which new wartlike lesions had soon reappeared.

DISCUSSION

Dr. STILLIANS was impressed with the appearance of the general angioma of bluish color, but could offer no explanation for the central hypertrophic development.

Dr. PUSEY said that he had seen an angiokeratoma somewhat like this.

Dr. COLE called attention to the fact that some of the angioma lesions had become necrosed. It looked like an angiokeratoma, but he had never seen one on the thigh.

Dr. FISCHKIN said that most of the angiokeratomas were described as occurring in erythematous skins due to chilblains, but in this case it had formed on the nevus, which was unusual.

Dr. ORMSBY presented a photograph of malignant pustule, taken about six weeks previously, which resulted from the use of an infected shaving brush. The micro-organisms of anthrax were demonstrated without difficulty in serum from the lesion, and the brush was found to be infected. The patient had

purchased a new brush and had only used it twice when he developed the disease. He was treated with anti-anthrax serum and made a good recovery. When first seen he had a temperature of 105 F. and was desperately ill. Treatment was instituted immediately, and he began to improve. No surgery was employed and nothing but an antiseptic retention dressing was applied to prevent the micro-organisms from being carried to others. The brush used by the patient, together with others of the same manufacture, were taken in charge by the State Board of Health.

DR. PUSEY said he thought all the cases found during the war had been shown to be due to brushes made of Oriental hair, and the infection did not occur in the better grade of shaving brushes—the more expensive ones.

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DISSEMINATION OF SPIROCHAETA PALLIDA IN EXPERIMENTAL SYPHILIS *

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The earliest studies of Schaudinn and Hoffmann¹ pointed to a rapid invasion of the lymphatic glands by *Spirochaeta pallida*. Metchnikoff and Roux² and Finger and Landsteiner³ were able to inoculate animals with lymph glands taken early in the course of infection. It was not until later that evidence was shown that in the absence of a primary lesion, spirochetes could be found in the circulation. For this discovery we are indebted to Reasoner,⁴ who, in 1916, demonstrated a generalized infection in rabbits from which the inoculated testicles had been removed before an initial lesion had fully developed. The obvious deduction from this study is that the dissemination of spirochetes occurs very early in the disease and that the primary focus of infection is not a measure of any subsequent reaction in the animal. Indeed, Reasoner found by experiment that the blood serum of an intratesticularly inoculated rabbit was capable of developing syphilis in other rabbits seventeen days before an initial lesion was palpable. These findings should be of value in establishing whether or not *Spirochaeta pallida* is present in experimentally infected animals, as for example, when the testes, following injection of material, remain negative macroscopically and also microscopically in dark-field examinations. With a view to confirm these observations in the course of routine work in latent syphilis, and to throw some light on the behavior of certain strains which have been isolated from different sources, experiments were

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1. Schaudinn and Hoffmann: Arb. a. d. k. Gsndhtsamte **22**:527, 1905.

2. Metchnikoff and Roux: System of Syphilis, ed. by D'Arcy Power and J. K. Murphy, 1914, Vol. 1.

3. Finger and Landsteiner: Arch. f. Dermat. u. Syph. **81-82**:147, 152, 1906.

4. Reasoner, M. A.: Some Phases of Experimental Syphilis with Special Reference to the Question of Strains, J. A. M. A. **67**:1799 (Dec. 16) 1916.

performed to determine roughly the presence of *Spirochaeta pallida* in the blood stream and regional lymphatic glands prior to manifestations of syphilis in the inoculated testicle of rabbits.

SPIROCHAETA PALLIDA IN LYMPH NODES AND BLOOD STREAM

Nov. 17, 1919, a strain of *Spirochaeta pallida*, isolated originally from a primary chancre on the penis, was injected into the left testicle of Rabbit 170.

Nov. 24, 1919, the testis was punctured and dark-field examination was negative. The testicle was normal. Five c.c. of blood were bled from the heart and the left inguinal node was excised. The left testicle of Rabbit 171 was injected with 2 c.c. defibrinated blood from Rabbit 170. The left testicle of Rabbit 172 was injected with 2 c.c. salt solution suspension of macerated lymph gland of Rabbit 170.

Nov. 27, 1919, the testicle was normal. Dark-field examination was negative. Five c.c. of blood were bled from the heart and 2 c.c. of defibrinated blood were injected into the left testicle of Rabbit 173.

Dec. 16, 1919, the testicle was normal. Dark-field examination was negative. Five c.c. of blood were bled from the heart and 2 c.c. of defibrinated blood were injected into the left testicle of Rabbit 174.

Dec. 20, 1919, the left testicle was enlarged and indurated. Dark-field examination revealed enormous numbers of spirochetes. The incubation period was thirty-five days.

RESULTS OF INOCULATION WITH BLOOD

Rabbit 171: Nov. 24, 1919, Rabbit 171 was injected left intratesticularly with 2 c.c. of defibrinated blood from Rabbit 170 (seventh day after inoculation).

December 18, a small nodule was palpable at the site of inoculation. Dark-field examination of puncture material from the testicle revealed numerous spirochetes. The incubation period was twenty-five days.

Rabbit 173: Nov. 27, 1919, this rabbit was injected left intratesticularly with 2 c.c. of defibrinated blood from Rabbit 170 (tenth day after inoculation).

Jan. 4, 1920, the testis was somewhat enlarged and indurated. Numerous spirochetes were present. The incubation period was forty days.

Rabbit 174: Dec. 16, 1919, this rabbit was injected left intratesticularly with 2 c.c. of defibrinated blood from Rabbit 170 (thirtieth day after inoculation).

Jan. 21, 1920, a small nodule, the size of a pea, appeared at the site of injection. Spirochetes in great numbers were present in the fluid from the testicle. The incubation period was thirty-six days.

RESULT OF INOCULATION WITH LYMPH GLAND

Rabbit 172: Nov. 24, 1919, this rabbit was injected left intratesticularly with 2 c.c. of salt solution suspension of the left inguinal gland taken from Rabbit 170 on the seventh day after inoculation.

December 20th, the testicle was markedly indurated. Dark-field examination of puncture fluid material from the testicle revealed numerous spirochetes. The incubation period was twenty-seven days.

In the absence of lesions and with negative dark-field findings in the testicle of a rabbit, the blood was found to contain *Spirochaeta pallida* seven, ten and thirty days after intratesticular inoculation, corresponding to twenty-six, twenty-three and three days prior to the appearance of an initial lesion. The regional lymph gland was also found to contain *Spirochaeta pallida* as early as seven days after inoculation of the testicle and twenty-six days before the rabbit had developed a lesion at the site of injection.

SPIROCHAETA PALLIDA IN THE SPLEEN OF EXPERIMENTALLY
INJECTED RABBITS

Although the organism causing syphilis may be absent from the blood stream, the liver, spleen and bone marrow may harbor spirochetes in great numbers. Elliot and Wile,⁵ in a study of 100 cases of early syphilis, found that the spleen was the first organ to be enlarged. Of these cases, a considerable percentage showed palpable splenic tumors. Splenic puncture yielded spirochetes. It had been shown by other investigators, notably by Zabolotny⁶ (1906) and Uhlenhuth and Mulzer,⁷ that the spleen and liver contain *Spirochaeta pallida*.

At a time when testicular lesions have disappeared and repeated dark-field examinations prove negative, it is of interest to determine whether or not *Spirochaetae pallidae* are still present elsewhere in the animal body. This point has considerable bearing on the question of latency in syphilis, and an experiment was devised with the object of studying the infectivity of the spleen under these conditions.

April 12, 1920, Rabbit 296 was injected intratesticularly with 0.2 c.c. salt solution suspension of *Spirochaeta pallida* (fourth generation of a strain isolated originally from the inguinal gland of a latent syphilitic).

May 20th, there was slight induration of the testes. Numerous spirochetes were present. The inoculation period was twenty-nine days.

5. Wile, U. J.: Am. J. Syph. 1:84 (Jan.) 1917.

6. Zabolotny: Centralbl. f. Bakteriologie. Ref. 38:13, 1905.

7. Uhlenhuth and Mulzer: Berl. klin. Wchnschr. 49:153, 1912; *ibid.* 50:2031, 1913; Centralbl. f. Bakteriologie, Orig. 64:165, 1912.

July 2nd, a few spirochetes were still demonstrable in puncture material from the testis.

From July 9th to September 11th, the testis was apparently healed; no lesions were visible, and there were no palpable nodules. Dark-field examination was negative.

September 11th, an emulsion of the entire spleen was prepared by maceration and straining through a heavy gauze filter. Dark-field examination of material was negative. Two c.c. of emulsion were injected into Rabbits 282 and 305. The testicle of Rabbit 296 was excised and injected into two normal rabbits, with negative results.

October 12th, Rabbit 305 presented a minute nodule in the lower pole of the testis. Puncture fluid was positive for *Spirochaeta pallida*. No perceptible change was noted in the testis, other than the small focal infection. The incubation period was thirty days.

November 30th, in Rabbit 282 there was marked induration of the entire testicle. Spirochetes were present in enormous numbers in the testicular fluid. The incubation period was eighty-one days.

It has been possible to recover *Spirochaeta pallida* from the spleen of a rabbit more than two months after the originally infected testicle has healed and been found negative for spirochetes by puncture and in vivo cultivation. The incubation period was about the same as that in the preceding generation of the same strain of organism. For the recovery of strains which appear to have been lost in passage through the testicle of rabbits, this technic can be employed to advantage.

DISCUSSION

The recovery of *Spirochaeta pallida* from the inguinal lymph glands and the blood stream of experimentally infected rabbits at a time when initial lesions have not yet appeared, points to a rapid invasion on the part of the organisms and offers a method by which diagnosis of suspicious material may be facilitated through animal inoculation. Wile⁵ reported some time ago the presence of *Spirochaeta pallida* in the testicle of a rabbit a few days after inoculation and at a time when no primary lesion had developed. This observation has a direct bearing on the application of a confirmatory test for demonstrating *Spirochaeta pallida*.

A recent contribution by Brown and Pearce⁸ established beyond cavil the fact that a syphilitic infection is not to be regarded as limited to the portal of entry. Even as early as forty-eight hours after inoculation of the testicles of rabbits, inguinal lymph glands were found

8. Brown, W. H., and Pearce, Louise: A Note on the Dissemination of *Spirochaeta Pallida* from the Primary Focus of Infection, Arch. Dermat. & Syph. 2:470 (Oct.) 1920.

to contain spirochetes with which it was possible to infect animals. Early invasion of the blood stream was demonstrated by experimental infection with blood obtained from rabbits one week after scrotal inoculation.

The bearing which these observations have on the problem of latency in syphilis is apparent both from these controlled experimental studies and clinical findings. It is highly probable that *Spirochaeta pallida* localize in certain foci, may be discharged into the blood stream from time to time and set up focal infections elsewhere in the body.

As a corollary to the deductions which may be drawn from the experimental findings reported, interpretation of the results should have considerable bearing on the question of the life cycle of *Spirochaeta pallida*. One of the strongest arguments offered in favor of an intermediary stage, simulating the protozoan parasites, has been the fact that spirochetes have never been recovered or seen during the incubation period within the rabbit testicle.

In the absence of convincing proof, other than microscopically negative findings, a better demonstration of the presence of unaltered *Spirochaeta pallida* cannot be offered than that of early invasion of the regional lymph glands and the blood stream. The chances are rare of seeing the few organisms which may be present early in the period of incubation, and the burden of proof should rest with those who have found it expedient to interpret negative findings as a basis for a far-reaching theory which had no fact to substantiate it.

SUMMARY AND CONCLUSIONS

Spirochaeta pallida have been isolated from the blood stream of experimentally infected rabbits, seven, ten and thirty days after intratesticular inoculation, at times corresponding to twenty-six, twenty-three and three days prior to the appearance of any initial lesion.

The regional lymph glands of rabbits have been found to contain active virulent *Spirochaeta pallida* seven days after inoculation of the rabbit's testicle and twenty-six days before any primary lesion had appeared.

The spleen has been shown to contain *Spirochaeta pallida* more than two months after the inoculated testicle had healed entirely and has been found free from spirochetes by repeated puncture and direct inoculation of the excised testicle into other rabbits. For confirmation of experimental work and for the diagnosis of suspicious syphilitic material which cannot be studied microscopically, it appears that the method suggested by these studies might be employed to advantage.

With early invasion of the lymph glands and blood stream established definitely during the incubation period of syphilis in animals, the

theory of a life cycle of *Spirochaeta pallida* is weakened considerably. The absence of organisms, as judged solely by microscopic findings, is not convincing proof that a change of form has taken place within the animal body. That *Spirochaeta pallida* is found unaltered both in morphology and in virulence in the blood and glands seems sufficient to render the theory untenable.

VISCERAL SYPHILIS

SYPHILIS OF THE SPLEEN *

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SYPHILIS OF THE SPLEEN

Syphilis of the spleen, giving rise to symptoms, which is an exceedingly common finding in syphilis of the new-born, and a not infrequent pathologic finding in recent syphilis, is thought to be relatively rare in acquired syphilis. It is far more frequent in the earlier stages of the infection, occurring coincident with the general lymphadenitis, than as the later or tertiary form. The relative insensibility of the organ under normal conditions and the absence of symptoms referred to it, often when it is pathologically affected, make it seem probable that it is the site of disease in connection with syphilis more frequently than is indicated by the literature. Clinical syphilis of the spleen occurs early, in the form of acute splenic tumor with or without pain, late as interstitial splenitis, as solitary or miliary gummas and as amyloid disease of the spleen. In addition, the spleen is frequently enlarged as a result of interstitial splenitis and perisplenitis in association with visceral syphilis elsewhere. Mention has already been made of isolated cases of syphilis of the liver in which the spleen is enormously enlarged, simulating the picture of Banti's disease.

SPLENIC HYPERTROPHY IN EARLY SYPHILIS

(Syphilitic Splenomegaly)

Incidence.—As a clinical entity, splenic enlargement in association with the earlier manifestations of syphilitic infection, was first noted by Biermer¹ in 1862. In 1874, A. Weil² published observations on splenic hypertrophy in acute syphilis. Similar observations are recorded by Gold,³ Columbini,⁴ Bruhns,⁵ Wewer,⁶ Haslund,⁷ Nolte,⁸ and Avan-

* Studies and Contributions of the Department of Dermatology and Syphilology of the University of Michigan, service of Dr. Udo J. Wile.

1. Biermer: Sweitz. Ztschr. f. Heilk. **1**:118, 1862.

2. Weil, A.: Deutsch. Arch. f. klin. Med. **13**:317, 1874.

3. Gold: Vrtljschr. f. Dermat. u. Syph. **12**:463, 1880.

4. Columbini: Istituto Dermosifilopatico della Universita di Siena, 1895, cited by Bruhns.

5. Bruhns: Deutsch. Arch. f. klin. Med. **64**:450, 1899.

6. Wewer: Deutsch. Arch. f. klin. Med. **17**:459, 1876.

7. Haslund: Arch. f. Dermat. u. Syph. **14**:346, 1882.

8. Nolte: Inaugural Dissertation, Greifswald, 1883.

zini.⁹ In an extensive study of early cases of syphilis, Elliott and I¹⁰ found splenic tumor in over 36 per cent. of the cases studied. In this series of cases, the determinations were made by palpation alone. We determined, moreover, that enlargement of the spleen may occur even before secondary dissemination, and that splenic enlargement probably represents the earliest syphilitic visceropathy. Soukernik,¹¹ in a similar study, found splenic enlargement in thirty-seven of sixty-one cases examined, and pain in six of these.

Symptoms.—Usually enlargement of the spleen at this stage of the disease is symptomless. This accounts for the fact that it is not more frequently observed. The occasional anemia and digestive disturbances which were sometimes noted in association with the enlargement by Neumann¹² and by Elliott and myself, are probably not part of the enlargement of the spleen itself, but belong rather to the constitutional infection.

Pain.—Pain as a rule is absent, but was found in six of our cases and is noted also by other authors. In one case observed by myself, abdominal pain referable to the spleen was the chief cause of complaint. In this case it was exquisite and was promptly relieved by antisyphilitic treatment.

Tumor.—Of thirty-six cases in the series observed in my clinic, nineteen were soft; the spleen extended well below the costal margin; the edge was rounded and the enlargement was similar to that found in typhoid or other general infections. The remainder were firm, readily palpable and similar to the interstitial splenitis of chronic malaria.

Blood Findings.—In twenty-seven cases in which the blood was carefully studied in Elliott's and my series, fourteen showed a leukocytosis of over 10,000.

Course.—In untreated cases the spleen may become permanently enlarged, and the early syphilitic hypertrophy may develop into chronic interstitial splenitis. Under the influence of treatment, however, the spleen rapidly decreases in size. The pain is almost instantly relieved by treatment. In a few cases in our series, notwithstanding vigorous treatment, the spleen remained constantly enlarged as late as one year after treatment. We were able thus to trace the course of the disease from an early splenitis to an interstitial type.

Prognosis.—The prognosis for restitutio ad integrum rests on the early diagnosis. I am inclined to think that the readiness with which

9. Avanzini: Vrtljhr. f. Dermat. u. Syph. **16**:379, 1884.

10. Wile and Elliott: Am. J. M. Sc. **150**:512, 1915.

11. Soukernik: Thèse de Paris, 1896.

12. Neumann: Spez. Path. u. Therap. in Nothnagel **23**:440, 444 and 446.

early splenic enlargement becomes converted into interstitial splenitis, without treatment, has a decided bearing on the future prognosis of the disease, although there is little data bearing on this subject. As a lymphatic structure and one having such an intimate relation to the blood stream, it is not inconceivable that the spleen in cases of chronic syphilitic splenitis serves as a depot for further distribution of spirochetes. As such, acute splenic tumor might well have an important bearing on the prognosis of late syphilis.

Treatment.—The treatment is that of constitutional syphilis.

LATE SYPHILIS OF THE SPLEEN

Late involvement of the spleen is exceedingly rare, both clinically and pathologically, as compared with syphilis of other organs. Interstitial splenitis, described first by Virchow,¹³ and a common finding in hereditary syphilis, gummosis splenitis and amyloid disease, are the pathologic types noted.

INTERSTITIAL SPLENITIS

This seldom occurs alone, at least clinically, but is most frequently found in association with syphilis of the liver, syphilis of the kidneys and of other viscera. The form in which it occurs is identical with that in cases of broken compensation and of cirrhosis of the liver. Reference has already been made to cases of chronic splenic tumor simulating primary splenomegaly and cases of syphilitic cirrhosis in which the enlargement of the spleen is the dominant, striking entity. Martland¹⁴ has described an interesting case of syphilitic cirrhosis of the spleen in association with general amyloid changes. A parenchymatous splenitis clinically apparent as a soft chronic enlargement is described also by Virchow. As a clinical entity alone, I believe it has not been recognized, but is principally the subject of an occasional pathologic report.

Symptoms.—Except for the increase in size, there are absolutely no clinical manifestations associated with chronic interstitial splenitis. In a few cases in which the increase is great, enlargement in the abdomen is noted. In those cases simulating Banti's disease, the tumor, and occasionally acites, may be striking features. To palpation, the spleen is usually firm, resistant and occasionally slightly tender. Gastro-intestinal symptoms sometimes found are usually referable to syphilis of the liver or other associated visceropathies. According to Neumann,

13. Virchow: Virchows Arch. **15**:319, 1858; Ueber die Natur der Constitutionell Syphilitischer Affectionen, *ibid.*, 1859.

14. Martland: Reprint, City Hospital Medical and Surgical Reports. Presented to the New York Pathological Society, 1908.

it is difficult to point out the part played by interstitial splenitis in associated syphilitic anemia. As chronic interstitial splenitis may occur without marked change in the blood stream, it is more than likely that the anemia and the blood changes are related more particularly to bone marrow changes than to the changes in the spleen itself.

Diagnosis.—Diagnosis is possible only in the presence of a large, firm tumor in which all other causes of splenic enlargement may be excluded. In the presence of other syphilitic manifestations, and with a positive Wassermann test, chronic enlargement of the spleen is no longer so difficult of recognition as syphilitic splenitis, as previously stated by earlier writers. In those cases in which the spleen is not sufficiently enlarged to palpate, the diagnosis *intra vitam* is impossible.

Prognosis.—The prognosis for disappearance of the tumor is not good. The association of other visceropathies, particularly of amyloid disease of the spleen and liver, of syphilitic disease of the liver itself other than amyloid disease, makes the prognosis unfavorable, not necessarily for the splenitis itself, but for the general syphilis of which the interstitial splenitis is a part.

GUMMATOUS SPLENITIS

This form is common in syphilis of the new-born, but exceedingly rare in acquired syphilis. In a large number of cases of late syphilis, I have not seen one case of clinical gummatous splenitis. Isolated cases are described by Rokitansky,¹⁵ Virchow, Wagner,¹⁶ Neumann, Pihan du Feillay,¹⁷ Gregoric,¹⁸ Gold, Litten,¹⁹ Cooper Forster,²⁰ Deguy²¹ and others. Most of these, however, were studied pathologically and were not recognized as clinical entities. Two forms are described—the large gummatous form which manifests itself clinically as a diffuse enlargement of the spleen in which there are palpable gummatous nodes, varying in size from that of a pea to that of a walnut, and miliary gummas. The first form is clinically recognizable. The second form is recognizable pathologically only. In the latter case the organ itself may or may not be generally enlarged, and the syphilitic nature of the disease is demonstrated only at the postmortem examination. The gummatous form may occur in association with amyloid disease of the spleen or as a part of interstitial splenitis.

15. Rokitansky: *Lehrbuch der Pathologisch. Anatomie* 3:254, 1855.

16. Wagner: *Arch. d. Heilkunde*, 1863, p. 430.

17. Fiellay, Pihan du: *Union Medicine*, 1862, cited by Robert, *Thèse de Paris*, 1905.

18. Gregoric: *Memorabilin Heilbronn*. 15: No. 3, 1870.

19. Litten: Cited by Neumann, p. 446.

20. Forster, Cooper: *Med. Times and Gaz.*, London, 1862.

21. Deguy: *Thèse de Paris*, 1900.

AMYLOID DISEASE

There is nothing in the clinical picture of amyloid disease of the spleen due to syphilis which in any way distinguishes it from amyloid disease due to other causes. Not infrequently, as has been mentioned in the foregoing, there are associated gummatous lesions in the spleen itself, in which case the diagnosis is simplified. Amyloid disease of the spleen can be recognized clinically as such in the presence of amyloid changes in the intestine or in the viscera. The syphilitic nature of such amyloid changes may be presumed when, in addition, the Wassermann test is positive. Usually, however, amyloid disease due to syphilis, like miliary gummas of the spleen, is a pathologic entity rather than a clinical one.

VISCERAL SYPHILIS

SYPHILIS OF THE PANCREAS *

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The pancreas is a common site of election for syphilis of the new-born, but clinical syphilis of the pancreas in the acquired form must be regarded as one of the rarest of visceral manifestations. Rokitan-sky¹ was the first to call attention to the occasional association of syphilitic pancreatitis with syphilitic hepatitis. Later Lancereaux² mentions its association also with other forms of visceral syphilis. Cases demonstrated at necropsy, in which the diagnosis was not suspected *intra vitam*, have been reported by Chvostek,³ Drozda,⁴ Schlagenhauser,⁵ Steinhaus,⁶ Rosenheim,⁷ Kovacs,⁸ and Luret and Secousse.⁹ According to Neumann,¹⁰ the diagnosis is practically never made during life, or at least without operation. I have been able, however, to find a number of cases in which undoubted syphilis of the pancreas was diagnosed *intra vitam*. Such cases are reported by Moynihan,¹¹ Michaloff,¹² Singer,¹³ Wolff,¹⁴ Trinkler,¹⁵ Jevinici,¹⁶

* Studies and Contributions of the Department of Dermatology and Syphilology of the University of Michigan, service of Dr. Udo J. Wile.

1. Rokitansky: Lehrbuch der Pathologische Anatomie **3**:254 and 255.
2. Lancereaux: Traite de Syphilis, 1874, p. 254.
3. Chvostek: Wien. med. Wchnschr. 1877, No. 33.
4. Drozda: Wien. med. Presse, 1880.
5. Schlagenhauser: Einfall von Pankreatitis syphilitica indurativa et gummosa aquisita, Arch. f. Dermat. u. Syph. **34**:44, 1895.
6. Steinhaus, cited by Walter-Sallis, reference No. 20: Soc. Anat. Path. du Belge, 1907.
6. Steinhaus: Soc. Anat. Path. du Belge, 1907.
7. Rosenheim: Ueber Einen Fall von Chronischen Interstitiellen Pankreatitis, Berl. klin. Wchnschr., No. 35:317, 1898.
8. Kovacs, cited by Zerfing, Southern Calif. Practitioner **23**:199, 1908.
9. Luret and Secousse: Sur un cas de syphilis tertiaire du pancréas s'accompagnant de compression de la veine porte, Gaz. hebdomadaire de médecine et de chirurgie, **35**:104, 1914.
10. Neumann: Syphilis, Spezielle Pathologie und Therapie, in Nothnagel's System, Ed. 2, 1899, p. 433.
11. Moynihan: Some Cases of Chronic Pancreatitis, Lancet, No. 2:856, 1902.
12. Michaloff, cited by Charmaux, Thèse de Paris, 1894.
13. Singer, G.: Zur Klinik der kronischen Pankreasaffektionen, Wien. med. Wchnschr. **60**:2605, 1910.
14. Wolff, E.: Pankreascysten u. Pseudocysten, Beitr. z. klin. chir. **74**:487, 1911.
15. Trinkler, N.: Zur Diagnose der Syphilitischer Affektionen des Pankreas, Deutsch. Ztschr. f. Chir., No. 75:58, 1904.
16. Jevinici, cited by Walter Sallis, Ann. de dermat. et syph., Ser. 5, **4**:665, 1913.

Umber,¹⁷ Kretschmer¹⁸ and Strauss.¹⁹ With the exception of Walter Sallis,²⁰ clinicians agree that the condition is exceedingly rare. Of 188 cases of pancreatic disease studied by Oser,²¹ only three were cases of pancreatic syphilis. Walter Sallis, however, who has written an extensive monograph on the subject, asserts that the condition is not so rare, and cites the fact that syphilitic lesions occurred in the pancreas forty-five times in 100 cases of abdominal syphilis. He was able, however, to collect only fifteen cases of clinical pancreatitis. The belief in the rarity of the condition as outlined above is not shared by Warthin,²² who, in an article written in 1916 and in subsequent publications, says that he believes that chronic interstitial pancreatitis is one of the most frequent visceropathies found at necropsies in cases of latent syphilis. He states that syphilis is the most common cause of interstitial, interlobular and interacinar pancreatitis, and suggests an etiologic relationship between such pancreatitis and diabetes mellitus.

INCIDENCE

According to most authors, syphilis of the pancreas occurs in a sclerous and a gummatous form. I have, however, been able to find two cases in which definite cysts occurred, undoubtedly due to the absorption of gummatous lesions. The condition occurs, therefore, as a gummatous or nodular pancreatitis and as an interstitial pancreatitis. A combination of both of these forms is also found.

SYMPTOMS

The symptoms of syphilitic pancreatitis differ but slightly from those of other pancreatic diseases. For this reason, according to Neumann, a differential diagnosis is almost impossible. A careful scrutiny, however, of the few cases reported shows some slight differences in the symptomatology from other forms of pancreatic disease in a few cases. Most cases are indistinguishable as syphilitic. The pancreas is so seldom alone involved that the symptoms are frequently masked by those of involvement of the adjacent viscera.

17. Umber: *Zur Viszerale Syphilis (Pankreatitis syphilitike mit Diabetis, akute gelbe Leberatrophie und ihrer heilung durch Salvarsan)*, München. med. Wchnschr. **58**:2499, 1911.

18. Kretschmer, J.: *Die Vielgestaltigkeit der Viszerale Lues*, Deutsch. med. Wchnschr. **36**:835, 1910.

19. Strauss, H.: *Hochgradige Pankreas-Atrophie bei Diabetis*, Berl. klin. Wchnschr. **48**:40, 1911.

20. Sallis, Walter: *Ann. de dermat. syph.*, Ser. 5 **4**:657, 1913.

21. Oser: *Ztschr. f. klin. Med.* **26**:191, 1894.

22. Warthin: *Syphilis of the Pancreas, with Reference to the Coincidence of Syphilitic Pancreatitis and Diabetes*, Tr. Assn. Am. Phys. **31**:387, 1916.

Pain.—As in other cases of pancreatic disease, pain is a predominating symptom. It has, however, no characteristic. In some cases it is identical with that of cholelithiasis, radiating to the shoulder and suggesting in its paroxysmal character, typical gallstone colic.

Functional Disturbance.—Functional disturbance of the pancreas has been noted in a few cases. Rosenheim⁷ and Umber¹⁷ report practical absence of protein digestion and associated fatty stools. Fat in the stools is also recorded in one of the cases reported by Singer.¹³

Glycosuria.—Glycosuria occurred in eight cases, and Walter Sallis²⁰ insists that syphilis of the pancreas is distinctly "diabetogenous." He also mentions steatorrhea as strongly suggestive of pancreatic syphilis. Glycosuria is usually slight; in a few cases it is severe, the percentage being as high as 7.6 in one case reported by Wolff.¹⁴ Maltosuria occurred in one case reported by Rosenheim.⁷

Fever.—Fever occurred in a fair percentage of the cases mentioned and is also of some diagnostic value as differentiating chronic pancreatitis.

Tumor.—Of the fifteen cases collected by Walter Sallis,²⁰ tumor occurred in eight, and therefore must be considered as a suggestive finding in syphilis of the pancreas. Emaciation is present in a few cases, but is never so severe as in malignant neoplasm.

Icterus.—Icterus was found in almost every case of pancreatic syphilitic disease. It may be due to pressure on the common duct by a gumma of the head of the pancreas or as frequently may be due to associated hepatic syphilis. Clay colored stools are reported in those cases in which obstructive jaundice occurred.

Gastro-intestinal Disturbances.—Vomiting and nausea, fat diarrhea, meteorism and colic occur as they do in other forms of pancreatic disease.

To sum up, there are no direct pathognomonic symptoms of syphilis of the pancreas. The few points suggestive of syphilis when the pancreas is the seat of the disease are jaundice without other cause, glycosuria and tumor of the pancreas without cachexia.

DIAGNOSIS

The differential diagnosis is extremely difficult. The cases must be distinguished from carcinoma of the head of the pancreas, from cholelithiasis and from chronic interstitial pancreatitis. Except for the predominance of glycosuria in syphilis (in about 50 per cent. of the cases) and the relatively mild cachexia in association with large palpable tumor, there are no definite criteria to differentiate syphilis of the pancreas from other forms of pancreatic disease. The association, however, of hepatic disease, or of any other form of syphilis, points

strongly toward syphilis as the cause of pancreatic disease when such can be demonstrated; and it is worthy of note that most of the cases of pancreatic disease have been associated with other forms of syphilis. Lastly, the therapeutic test has proved the most efficient diagnostic aid in the majority of cases.

PROGNOSIS

According to Neumann,¹⁰ the prognosis is unfavorable, as most of the cases are recognized only during the postmortem examination. With, however, the routine Wassermann test performed on all patients, the prognosis should be more favorable. In the cases that I have been able to collect from the literature, complete recovery is reported as a result of the administration either of arsphenamin, mercury or iodid, or of mercury and iodid combined, in ten cases: those of Moynihan,¹¹ Michaloff,¹² Wolff,¹⁴ Trinkler,¹⁵ Jevinici,¹⁶ Umber,¹⁷ Kretschmer¹⁸ and three of Singer's¹³ cases.

SECONDARY SYPHILITIC INFECTION *

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The disinclination to admit the possibility of a second infection with syphilis in a patient in whom the acquired disease has become generalized is fortified by clinical experience of many years. A few doubtful cases might be cited, but the preponderant weight of the opinion of the medical profession has been against such an interpretation of the facts presented. We are still ignorant of the explanation of the resistance of the tissues of a syphilitic patient to infection from without, while susceptible to local infection from within, especially as some of the late genital lesions often closely simulate a chancre.

If there have been so few, if any, authentic cases of reinfection, the explanation appears to be simple—there were few cases of radical cure. Some of the greatest authorities, notably Fournier and Hutchinson, believed, apparently, that they could eradicate the disease, and they certainly were able to follow some of their patients for many years and to see them remain apparently well themselves, and become the parents of healthy children. In view, however, of our present knowledge of the persistence of small foci of infection in the heart, aorta and other organs, with no clinical signs except a positive Wassermann reaction, we are justified in doubting the completeness of these cures. If it is true that the absence of cases of reinfection is due to the absence of cases of radical cure, it follows that if radical cure can be obtained, a certain number of cases of reinfection should occur. It may be, on the other hand, that the rarity or absence of cases of reinfection is due to a partial immunity which persists after the extinction of the infectious process, as in typhoid fever and in the exanthems. If this were true, a greater number of radical cures would not be followed by an increased number of cases of reinfection. The improvement in treatment which has occurred in the past ten years has been accompanied by a great increase in the number of reported and apparently authentic cases of reinfection, and it is increasingly probable, therefore, that resistance to reinfection is due to the presence of the disease itself, and not to an enduring immunity.

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The possibility that a patient with congenital syphilis may subsequently acquire the disease has never, so far as I know, been questioned. Indeed, this occurrence is constantly invoked to explain the apparent cases of syphilis of the third generation. Why should we admit the possibility of reinfection in a congenital syphilitic patient and deny such a possibility in a victim of the acquired disease? It would seem to be more reasonable to assume that in both cases the possibility depends on the extinction of the infection either by treatment or by the lapse of time. The question is: Do such reinfections occur? As absolute proof is difficult or impossible to obtain, we must decide by the balance of probability, and approach the question with an open mind. The following case, which occurred in the service of Prof. William B. Trimble at the University and Bellevue dispensary, is most easily explained, I believe, on the theory of reinfection.

REPORT OF A CASE

History.—Michael G., aged 27, when first seen, Aug. 9, 1916, gave a history of penile sore eight months previously, for which he had been treated with about twenty injections of mercury. He complained of headaches and pains in the extremities, and showed extensive mucous patches on both tonsils. The Wassermann reaction was ++.

Treatment.—Nine-tenths gram of neo-arsphenamin was administered Aug. 11 and Nov. 3, 10, 17 and 24, 1916. Nine-tenths gram of arsphenamin was administered July 6 and 0.6 gm. on July 20 and Aug. 3, 1917. Six-tenths gram of arsphenamin was administered March 1, 8, 15 and 22, 1918. Mercury in the form of intramuscular injections of the salicylate and mixed treatment internally, was given throughout the course, but the patient was a sailor, and the treatment was necessarily irregular. All symptoms disappeared under treatment. Wassermann Reaction: After the first test, this varied from negative to +, except on Feb. 18, 1918, when it was ++. Sept. 14, 1918, the reaction was negative, and three tests made in the army between Sept. and Dec. 15, 1918, were said to be negative.

Second Occurrence of Condition.—Nov. 19, 1919, the patient returned with a penile sore of four weeks duration, occurring on the site of the original primary lesion. The incubation period could not be established, as he had been exposed several times in the month preceding the appearance of the sore. The border was firm and the base indurated. The inguinal glands were enlarged. The Wassermann reaction was negative November 19, and again on December 3. Dark-field examination made November 19 revealed no spirochetes, presumably on account of the use of an antiseptic dressing. Microscopic examination on December 12 revealed both *Spirochaeta pallida* and the Ducrey bacillus.

DIFFERENTIAL DIAGNOSIS

In this case the diagnosis in the first instance was made both by clinical and by laboratory methods; treatment by both arsphenamin and mercury was faithfully, if somewhat irregularly, carried out; all symptoms—both clinical and serologic—disappeared; and although the

Wassermann reaction at the time was negative, exposure was followed by the development of a sore in which spirochetes were demonstrated. If this sore was not a chancre, what was it? Under the title "chancre redux," Fournier¹ describes a lesion clinically indistinguishable from a chancre, occurring on the site of a previous chancre, usually, within a week or two of the healing of the first. It is in reality a fresh ulceration in the induration remaining from the original sore. The case under discussion cannot fall in this category as the induration of the original sore had entirely disappeared, and the interval was two years instead of a few weeks.

Under the same title, "chancre redux," or "recurring chancre," Hutchinson² describes a lesion exactly resembling a chancre, which may occur after an interval of from a few months to several years, and which almost invariably occurs in the site of the primary lesion. He states that it is not attended by glandular enlargement and is not contagious, and adds: "Whether the cartilaginous induration should be classified as gummata is a question chiefly of definitions." Some of the cases were accompanied by tertiary symptoms in other parts of the body. The lesion described by Hutchinson as "chancre redux" had previously been described by Fournier³ as the pseudo-chancre induré, and the identity of the two is accepted by Hutchinson. The interval after the first sore varied from ten months to several years. Fournier insists that clinically, as far as the sores themselves are concerned, the chancre and the pseudo-chancre are indistinguishable, and his statement must be accepted as true. He agrees with Hutchinson that the satellite glands are seldom involved, but describes three exceptional cases among the twenty-one which form the basis of his report, in which such adenopathy occurred. In several cases there were other symptoms of syphilis present. Fournier states that the pseudo-chancre frequently occurs in the scar of the primary lesions, but he does not assert that this location is invariable. He gives the histories of three cases, in one of which the pseudo-chancre occurred on a different part of the penis, in another on the upper lip, and in the third on the scrotum. From the point of view of diagnosis, it therefore appears to be immaterial whether the two lesions involve the same area or not. These lesions are distinctly tertiary in type; that is, they are solitary localized ulcers, with little or no tendency toward glandular enlargement, and, according to Hutchinson, they are noncontagious. Fournier cites one case in

1. Fournier, A.: Etude clinique sur l'induration syphilitique primitive, Arch. gen. de méd., November, 1867.

2. Hutchinson: Syphilis, London, 1909, p. 171.

3. Fournier, A.: Du pseudo chancre induré des sujets syphilitiques, Arch. gen. de méd., June, 1868.

which the wife of the patient remained free of all symptoms of syphilis; he does not mention this point in regard to the others. This absence of contagiousness is to be expected, as it is usually the rule in late lesions.

It is possible that the case under discussion belongs in this group; absolute proof to the contrary is impossible. The case differs, however, in many important respects: First, the patient had received more vigorous treatment than either Fournier or Hutchinson were acquainted with. Second, he had no other symptoms of syphilis, as was true in some of the cases of pseudo-chancres; also, the Wassermann reaction was persistently negative. Third, the sore was infectious, as was shown by the presence of spirochetes. Fourth, the neighboring glands were enlarged and painless.

Of course, a tertiary lesion may simulate exactly the clinical appearance of a chancre; it may coexist with a persistent negative Wassermann reaction; it may be contagious, although the demonstration of spirochetes is rarely possible; and it may be accompanied by a satellite adenopathy; but all these unusual phenomena seldom occur in the same patient at the same time. It is more reasonable to believe that the man was cured and was reinfected. If the possibility of a cure is admitted, the case presents no difficulty.

CASES OF REINFECTION REPORTED IN THE LITERATURE

Within the last few years, the number of reported cases of reinfection has increased rapidly. Benario's⁴ monograph, published in 1914, gives complete details of ninety-six cases collected from the literature, of which forty-one satisfy the requirements which he considers necessary to establish a diagnosis of reinfection. Of the remainder, he considers that thirteen are probable and twenty-eight are possible cases of reinfection. Benario says that a diagnosis of reinfection must be based on: (1) a positive clinical diagnosis of the primary lesion, (2) demonstration of *Spirochaeta pallida*, (3) satellite adenopathy, (4) repeated performance of the Wassermann test, and (5) if possible, recognition of the source of infection. As in all cases in which judgment depends on weighing of evidence rather than on absolute demonstration, another observer might rearrange the cases in his various classes to a certain extent, but on the whole his opinion seems to be just. Since that time the number of reported cases has been considerably increased. The largest series that I have found was reported by White,⁵ who bases his cases on the following proof of reinfection: 1. In the first attack, spirochetes were found in the chancre or in syphilitic

4. Benario, J.: Samml. swangl. Abhandl. a. d. Geb. d. Dermat. d. Syph., etc. **3**:1, 1914.

5: White: Brit. M. J. **2**:509 (Oct. 20) 1917.

lesions, or the blood gave a positive Wassermann reaction (the positive Wassermann reaction of hereditary syphilis must be excluded). 2. In the second attack, the spirochetes were found in a new chancre, which appeared at a site different from that of the first chancre, the blood at the same time giving a negative Wassermann reaction. The author presents the histories of ten cases fulfilling these conditions, seen by himself in both attacks in an army hospital, occurring in a series of 10,500 cases of syphilis. He presents eighteen other cases which lack one or more of these requirements—usually either the record of a negative Wassermann reaction at the beginning of the second attack, or the demonstration of the spirochete. The treatment of the first attack usually consisted of eight injections of arsphenamin of 0.3 gm. each and from five to seven injections of mercurial cream, each containing 1 grain of mercury, at weekly intervals. The interval between the two attacks was short—seldom over a year. This short interval and scanty treatment throws some doubt on a series otherwise very convincing. It should be remembered, however, that treatment was begun early, and the amount given might well be effective in such cases, while it would be totally inadequate if begun at a later stage of the disease.

A somewhat cursory search of recent literature reveals reports of convincing cases by Jeanselme and Vernes,⁶ Gaston and Sanglier-Lamark,⁷ Milian and Sauphar,⁸ Parounagian,⁹ Sweitzer,¹⁰ Berent,¹¹ Deroide,¹² Pantou and Simpson,¹³ Spangenthal,¹⁴ Schamberg,¹⁵ Laurent,¹⁶ and Saraphi.¹⁷

A case reported by Lichtenstein¹⁸ and one reported by Irvine¹⁹ are probably both second infections, but as neither gives the record of a negative Wassermann reaction at or just before the beginning of the second attack, the evidence of a cure of the first infection is incomplete.

6. Jeanselme and Vernes: *Bull. Soc. franç. de dermat. et syph.* **22**:353, 1911.

7. Gaston and Sanglier-Lamark: *Bull. Soc. franç. de dermat. et syph.* **23**: 468, 1912.

8. Milian and Sauphar: *Bull. Soc. franç. de dermat. et syph.* **24**:7, 1913.

9. Parounagian: *New York M. J.* **103**:153 (Jan. 22) 1916.

10. Sweitzer, S. E.: *Reinfection in Syphilis*, *J. A. M. A.* **66**:1196 (April 15) 1916.

11. Berent: *München. med. Wchnschr.*, Sept. 26, 1916, p. 1408.

12. Deroide: *Bull. et mém. Soc. méd. d. hôp. de Par.*, Ser. 3, **41**:603, 1917.

13. Pantou and Simpson: *Brit. M. J.* **1**:535 (May 11) 1916.

14. Spangenthal, J.: *A Case of Syphilitic Reinfection*, *J. A. M. A.* **71**:730 (Aug. 31) 1918.

15. Schamberg: *J. A. M. A.*, Sept. 13, 1919, p. 826.

16. Laurent: *Bull. Soc. franç. de dermat. et syph.* **27**:15, 1920.

17. Saraphi: *Ann. d. mal. ven.* **15**:439, 1920.

18. Lichtenstein: *Wien. klin. Wchnschr.* **29**:1208 (Sept. 21) 1916.

19. Irvine: *Brit. M. J.* **1**:765, 1917.

In a case reported by Kermorgant,²⁰ the diagnosis of the first attacks rests on clinical evidence, and no secondary conditions were observed, except a polymicroadenopathy.

Two cases reported by Goubeau²¹ deserve more than passing notice. The first concerns a soldier who, in August, 1916, presented on the dorsum of the penis a typical chancre in which spirochetes were demonstrated, which healed under treatment with neo-arsphenamin and a silver preparation. On Dec. 13, 1916, the Wassermann reaction was negative, and the patient showed a typical indurated chancre at the extremity of the prepuce, with inguinal adenopathy. He denied exposure since July, and the author therefore believed this to be a pseudo-chancre; but as denial of exposure is not allowed to prevent a diagnosis of chancre in other cases, it should not be allowed to do so in this case. It is to be noted that the two lesions were 2 cm. apart. Goubeau's second case is one of evident reinfection. A man developed a chancre followed by typical secondary conditions in October, 1915. He received intensive mercurial treatment and two courses of arsphenamin of four injections each. There were no further symptoms, and the Wassermann reaction was negative. In November, 1916, after exposure, he developed a new chancre, with satellite adenopathy, followed after six weeks by roseola. It is not stated whether the two chancres were in the same or in different places, but as Fournier³ reports cases of pseudo-chancre occurring at sites different from that of the primary lesion, this detail hardly seems to deserve the attention that has been paid to it.

A decision as to the authenticity of any case of reinfection must, in the last analysis, rest on the weighing of probabilities. It must be acknowledged that tertiary lesions which are indistinguishable from chancres were in the same or in different places, but as Fournier by inguinal adenopathy, that it may be followed by an eruption of secondary character, that spirochetes may be demonstrated in the secretion, and that the Wassermann reaction may at the time be negative. Each of these occurrences is rare, and the chance that they should coexist is remote indeed. This coexistence, is however, possible, and as long as only a small number of cases of this nature were known, this explanation might be accepted. When the number of cases multiply, however, some explanation beyond mere chance combination is required. It may be that the occurrence of spirochetes in great numbers in a tertiary lesion would tend to produce satellite adenopathy, and that both would favor the development of relapsing secondary eruption, but we have no evidence of this, and it is hard to reconcile such a view with

20. Kermorgant: *Bull. et mém. Soc. méd. d. hôp. de Par.*, Ser. 3 **41**:886, 1917.

21. Goubeau: *Presse méd.* **25**:325, 1917.

the occurrence of a persistent negative Wassermann reaction. When a rapid increase in reported cases of this combination of symptoms is found to coincide with an epoch-making advance in efficacy of treatment, and especially when we note that this treatment has been followed in practically all cases reported, the conclusion is almost inevitable that the occurrence of the syndrome is dependent on the treatment, that is, that these are true cases of reinfection in patients who have been cured.

THE PHYSICAL BASIS OF RADIUM THERAPY

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RADIOACTIVITY

In the following paragraphs will be given a brief account of the most important physical factors involved in the therapeutic applications of radium. A complete presentation will not be attempted; only the essential points will be taken up somewhat in detail. Radium therapy has passed the preliminary stage of empiric experimentation, and is now recognized as an essential of the medical armamentarium.

The early history of radium is so well known that it is hardly necessary to dwell on it. It suffices to say that the property of radioactivity was discovered by Henri Becquerel in 1895, soon after the discovery of the roentgen rays by Roentgen, and that radium was discovered by Madame Curie in the same year. These discoveries "revolutionized" our ideas of physics and chemistry, in the popular sense of the word; but strictly speaking they did not. The laws of chemistry and physics are just as good today as they were before the advent of radium. The changes which the new knowledge brought about were simply extensions of our concepts of matter and energy. For instance, the atomic theory of matter was not overthrown but, on the contrary, received additional confirmation. The existence of atoms, originally a surmise, became an established fact. We can actually count atoms because we can count the alpha particles, which are positively charged helium atoms traveling at high speed. But our concept of the atom was greatly extended. Our preliminary assumption of the indivisibility of the atom had to be modified, since not only is the atom divisible, but it breaks up spontaneously. While we know little about the actual structure of the atom, we know that it must be very complex. The component parts are of electrical nature, some having positive and some negative charges. The negatively charged particles have a mass about two thousand times smaller than the hydrogen atom and are called electrons. The positively charged particles which have been examined so far are the alpha particles.

LIBERATION OF ENERGY IN RADIOACTIVE CHANGES

The phenomenon of radioactivity consists in the spontaneous change of one element into another, accompanied by the liberation of relatively enormous amounts of energy. The liberation of this energy is the most remarkable fact of radioactivity. It is on account of this

fact that radioactivity was discovered. The quantity of matter which changes in an appreciable period of time is small, but nevertheless we can detect the change on account of the large quantity of energy liberated. Thus 1 gm. of radium gives off 133 calories of heat per hour, which means that 1 gm. of radium will melt its own weight of ice in less than three quarters of an hour. In one year 1 gm. of radium gives off 1,160,000 calories. In that time it has lost only $\frac{1}{2500}$ part of its weight. In the complete change of 1 gm. of radium, 2,900,000,000 calories of energy are evolved, whereas in the formation of 1 gm. of water only 3,800 calories are liberated, and this is the chemical process which involves the greatest change of energy per unit mass.

CHANGE OF ONE ELEMENT INTO ANOTHER

The laws governing the change of one element into another have been worked out thoroughly by Rutherford and Soddy, who first formulated the theory of atomic disintegration. We have now the radioactive elements grouped into series, in which one element is the parent of the successive one. The most important of these series is the uranium series, of which radium and its subsequent products are part. This series is shown in the following table.

URANIUM SERIES

Element	Radiation	Half Value Period	Atomic Weight	Valency	Equilibrium Amount Mg.
Uranium 1.....	α	5 500,000,000 years	238	VI	3,140,000,000
Uranium X ₁	$\beta + \gamma$	24.6 days	234	IV	0.039
Uranium X ₂	β	1.15 minutes	234	V	0.00000125
Uranium 2.....	α	2,100,000 years	234	VI	1,210,000
Ionium	α	140,000 years	230	IV	81,000
Radium	α	1,730 years	226	II	1,000
Radium emanation...	α	3.85 days	222	0	0.0061
Radium A.....	α	3 minutes	218	VI	0.0000033
Radium B.....	$\beta + \gamma$	26.7 minutes	214	IV	0.000029
Radium C.....	$\beta + \gamma$	19.5 minutes	214	V	0.000021
Radium C'.....	α	0.000001 second	214	VI	Negligible
Radium D(Radio-lead)	Slow β	15.83 years	210	IV	9.16
Radium E.....	$\beta + \gamma$	48.5 days	210	V	0.077
Radium F (Polonium)	α	136 days	210	VI	0.077
End			206	IV	0.22

All the members of the series are true elements from the chemical standpoint. They have definite atomic weights, and react as elements in forming compounds. Each element preserves its identity as long as it lasts. The macroscopic change, that is, the change in the aggregate of the substance, takes place gradually, more or less rapidly according to the particular element. On the other hand, the microscopic or atomic change takes place suddenly. The law governing the change states that for any particular element the number of atoms disintegrating per unit of time is a definite fraction of the total number of

atoms of the element present at that time. The magnitude of this fraction depends on the rapidity with which the substance changes. Some substances change slowly, that is, a small number of the atoms present disintegrate in a finite interval of time; others change more rapidly.

It is customary in radioactivity to express the rapidity of change by what is known as the half value period of the element. This number represents the interval of time which must elapse for half of the initial amount of the element to disintegrate. It will be seen that this is a definite way of expressing the rapidity of the process because, no matter what the initial amount is, it will be reduced to one-half in that period of time. In twice that length of time the amount will be one quarter, in three times that length of time it will be one eighth of the initial amount, and so on. There is another way of expressing the rapidity of change of the radioactive elements, which in some respects is better—this is by giving the average life of the element. If we start with any given quantity of one element, a certain number of the atoms will remain atoms of that element up to a certain time, and then change into atoms of a different element. We can say that the life of these atoms has been this interval of time. Some atoms will break up at a later time, and therefore have a longer life, and some will live for a very long time. The number of atoms that have a short life is larger than the number of atoms that have a long life, and if we take the average of all these periods of life, we get the quantity that is called the average life of the element. This quantity is different for different elements. There is a mathematical relation between the average life and the half value period: average life = $1.43 \times$ (half-value period).

The energy that is given off in the radioactive change comes from the atom-itself. The higher the atomic weight the larger the quantity of energy associated with that atom. Since the radioactive change is from an element of a higher atomic weight to one of a lower atomic weight, there must be, perforce, an emission of energy. This energy manifests itself in the radiations, of which there are three distinct types, and as heat. For the moment it is sufficient to say that the alpha radiation consists of positively charged particles traveling at high speed which become helium atoms as soon as they take up two negative electrons. The beta radiation consists of negative electrons, also traveling at very high velocities. The gamma radiation is of electromagnetic nature, like the roentgen rays and ordinary light.

Referring to the accompanying table, we see that radium is the sixth element in the uranium series. It has an atomic weight of 226.

and a half value period of 1,730 years. One atom of radium, when it breaks up, expels an alpha particle and becomes one atom of radium emanation. We have, therefore, the change of one element into two distinct elements. Since helium has an atomic weight of 4, the atomic weight of radium emanation is equal to the atomic weight of radium minus 4, or 222. Radium is a metal closely related to barium, whereas radium emanation¹ is an inert gas, in the chemical sense of the word, like neon, krypton, etc. It has, therefore, zero valency. Radium, however, has a valency of 2, so it will be seen that the expulsion of an alpha particle results in the lowering of the valency by two. This holds in all changes which are accompanied by the expulsion of alpha particles.

The half value period of the emanation is 3.85 days. One atom of emanation breaks up, expels an alpha particle, and becomes radium A, which is again a solid. Similarly, radium A changes into radium B. In the change of radium B to radium C there is no expulsion of alpha particles, but instead beta and gamma radiations are given off. In this case, while we have the change of one element into another, there is no change in atomic weight. The valency, however, does change, and it will be seen from the table that the expulsion of a beta particle increases the valency by one. The transformation of radium C is rather complicated, because a branch product is formed. As, however, the amount of the branch product is only 0.03 per cent., we may say for all practical purposes that radium C changes into radium D, and that in this process alpha, beta and gamma radiations are emitted. The transformation goes on to radium F in a similar way, and from radium F or polonium a substance is formed which is indistinguishable from ordinary lead in its chemical behavior.

In the radioactive series of radium and its subsequent products we find that there is a wide variation in the half value period of the different elements. Radium emanation is produced slowly from radium, but it changes fairly rapidly into radium A. It is evident, then, that it cannot accumulate indefinitely. If we start with a given quantity of radium free of all subsequent products, the amount of emanation produced is the same as the amount of radium which disintegrates, and since radium changes slowly, the emanation is generated at substantially a constant rate. As soon as some emanation is formed, however, it begins to disintegrate, a definite fraction of the number of atoms present breaking up per second. In the beginning more atoms of emanation are formed than break up, and the

1. It is unfortunate that this new gas into which radium changes should have been called radium emanation, because it is easily confused by the layman with the radiations. The two things, however, are entirely different.

amount of emanation is therefore increasing. But as the number of atoms increases, the number which disintegrate per second also increases, so that a point will be reached at which the number of atoms which disintegrate per second is equal to the number which are produced per second. When this condition is attained we have what is known as radioactive equilibrium. From this time on, the quantity of emanation bears a definite relation to the amount of radium present. The amount of emanation in equilibrium with 1 gm. of radium is 0.006 gm. and occupies a volume of 0.06 c.mm. at normal pressure and temperature. The same mode of reasoning can be applied to the products which follow emanation, and we obtain thus the equilibrium amounts for the members of the series, shown in the table. For practical purposes in the case of radium and its subsequent products, the condition of equilibrium is reached in about thirty days. It is for this reason that the Bureau of Standards keeps radium tubes under observation for a few weeks before issuing a certificate. Their measurements are based on the gamma radiation from radium C, so that it is important for them to know what relation the amount of radium C which they measure bears to the amount of radium present in the preparation.

When we have radioactive equilibrium, the number of atoms disintegrating per second is the same at each step in the series. Therefore, for those changes in which alpha radiation is emitted, the number of alpha particles emitted at each step is the same. Since the activity of the substance is measured by the intensity of the radiations which it produces, it follows that the more rapidly changing substances are more radioactive, mass per mass, than those of slower change. This is an important fact to remember. It may be generalized by saying that the radioactive effect is proportional to the quantity of substance present divided by the average life of the substance. Thus, the shorter the life of the element, the more active it is.

RADIATIONS

We have described briefly three types of radiation which radioactive substances emit, the properties of which will now be discussed. The phenomenon of radioactivity was discovered accidentally, and it was discovered because the radiations affect a photographic plate. The photographic effect is common to all three types of radiation—alpha, beta and gamma. In general we can say that whatever one type of radiation does, the other types will do, to a greater or less extent. Besides the effect on the photographic plate, all three types have the power of producing luminescence, that is, if they fall on a suitable

substance, this substance will give off light which affects the retina. Phosphorescent zinc sulphid is made to glow beautifully by the alpha rays, but is little affected by beta and gamma rays. On the other hand, the fluorescence produced in willemite is mainly due to gamma and beta rays. The energy of all three types of radiation is transformed into heat energy, which can be detected, and even measured, by suitable instruments. The radiations produce chemical changes, decomposing and synthesizing substances. They also produce marked physiologic effects. The most important property of the radiations, however, is that of producing ionization, that is, of breaking up some atoms of a substance into positively and negatively charged particles. It is possible, and even probable, that all the other effects are brought about by ionization. For this reason we shall examine the question of ionization somewhat in detail.

Ionization.—When a beam of beta rays passes through a gas, some of the atoms of the gas are broken up into positively and negatively charged particles. The gas is then said to be ionized. To form a mental picture of ionization we may think of the beta particles as bullets flying through space. As the beta particles are extremely small, the intermolecular spaces are relatively large. Therefore there are only a few head-on collisions between the beta particles and the atoms, and few ions are produced in this manner. In general, however, when a beta particle comes into the sphere of influence of electrons within the atom, it may knock out an electron, losing some of its energy in the process. The free electron thus produced attaches itself to an atom or a cluster of atoms and is then called a negative ion. The remaining part of the atom, or the positive ion, may also collect a cluster of atoms around itself. In the process of ionization the beta particles do not usually lose all their energy in one collision, but rather a great many ions are produced by one beta particle. The greater the speed of the beta particle the more energy it has in the first place, and the harder it is for it to lose this energy in ionizing the gas, because it does not stay in close proximity to the electrons in the atom long enough to transmit some of its energy to them. This, of course, means that the greater the speed of the beta particles the more penetrating they are.

It is hard to form a mental picture of the passage of gamma rays through matter and the changes of energy that take place. We have already said that gamma radiation consists of electromagnetic disturbances similar to light waves. Like light, gamma rays have a definite wave length and travel with a speed of 186,000 miles per

second.² Physical considerations based on experimental evidence lead us to believe that the action of gamma rays is an indirect one. That is, the gamma radiation is first transformed into beta radiation, and the latter produces the effects which we observe. Thus in the case of ionization the passage of gamma rays through a gas causes some of the atoms to eject electrons at high speed. These secondary beta rays, as they are called, then ionize the gas, as explained above, for the primary beta rays. The number of ions produced directly by gamma rays, as they are called, then ionize the gas, as explained above, for the It will be seen, then, that most of the energy required to ionize the gas is transferred from the gamma radiation to the secondary beta radiation and from the latter to the atoms which are broken up.

Absorption of Radiations by Matter.—On account of this loss of energy by radiation, the intensity is less after the beam has traversed matter than it would be if the screen were not present. Matter then absorbs some of the radiation, and the energy thus taken up manifests itself in different ways. In living tissue it is this energy that is responsible for the changes brought about by the radiation. This question will be taken up in another paper. For the present we shall consider the absorption of the radiations by matter in a general way. All three types of radiation are capable of passing through matter. The alpha rays are easily absorbed even by very small thicknesses of solids or liquids, less than 0.1 mm. of aluminum being sufficient to block their passage completely. The maximum range in atmospheric air is about 7 cm. The beta rays are much more penetrating than the alpha rays, but not so penetrating as the gamma rays. The swiftest beta particles are capable of traversing 2 mm. of lead or nearly 1 cm. of aluminum, while gamma rays can be detected through 25 cm. of lead. In the composite radiation from radium, however, some gamma rays are less penetrating than the fastest beta particles. We may say that roughly beta rays are 100 times more penetrating than alpha rays and 100 times less penetrating than gamma rays. As over 90 per cent. of the energy emitted by radium is carried by the alpha particles, it will be seen that when radium or emanation is used in tubes, at best less than 10 per cent. of the energy is available for therapeutic purposes.

The absorption of beta rays per millimeter of any substance depends on the chemical constitution of the substance and on its density. The greater the density the larger is the absorption, and the higher the

2. It is to be noted that in electromagnetic waves the velocity of the propagation is the same for all, no matter what the wave length may be. The speed, therefore, has nothing to do with the penetration of the rays. This depends on the wave length—the shorter the wave length the more penetrating the rays.

atomic weight the larger the absorption, even though the density may be the same. Thus, mass per mass, lead is a much more efficient absorber of the beta radiation than aluminum. In the case of the gamma radiation, however, the absorption is nearly proportional to the density of a substance. Only elements of very high or very low atomic weight absorb a little more than elements of medium atomic weight.

Other Effects of Matter on Radiations.—In addition to absorbing some of the radiation, the presence of matter in the path of the rays causes other changes. When gamma rays impinge on a substance, the latter emits a secondary radiation of the gamma ray type, as well as of the beta ray type already mentioned. The corpuscular (or beta) radiation is always much more easily absorbed by matter than the primary radiation. But the higher the atomic weight of the screen, the more penetrating and more intense it is. The gamma radiation in general consists of two types: the general secondary radiation and the characteristic radiation. The former is heterogeneous and the wave lengths vary continuously from the short waves of the primary beam to much longer waves. On the whole, therefore, this radiation is more easily absorbed than the primary radiation. The characteristic radiation takes its name from the fact that its wave length depends solely on the element which is emitting it. It is produced only when the primary beam contains radiation of shorter wave length than the characteristic radiation of the element which is radiated. The higher the atomic weight of an element, the shorter the wave length of its characteristic radiation.

There is still another effect which the presence of matter has on the radiations. It is the phenomenon of scattering, or the irregular deviation of the rays in their passage through matter. Beta rays are easily scattered so that a beta particle, which in a vacuum would travel in a straight line, follows a zigzag path in matter. As a result, a cone of rays impinging on a slab of matter will have a larger aperture after traversing the screen. In fact, the radiation will be scattered in all directions, but the intensity in the forward direction is greatest. This is also true in the case of scattered gamma radiation.

THERAPEUTIC PROPERTIES OF RADIUM

The therapeutic properties of radium are due to its radiations, especially the beta and gamma radiations. The table indicates that the substances in the radium series which produce the beta and gamma radiations are descendants of radium emanation. Since radium emanation is a gas, it has a tendency to escape, so that in order to get the maximum beta and gamma radiation it is necessary to keep radium

in sealed containers. The radium then keeps up the supply of emanation in the tube, and this in turn keeps up the supply of radium A, B and C, which otherwise would decay rapidly. As the half value period of radium emanation is fairly long (3.85 days), it can be used as the primary source of radiation. In practice, the most effective way of utilizing radium is to collect its emanation in capillary glass tubes and use these tubes for the treatment of patients. With this method it is possible to do many things that cannot be done when radium salt is used as the source of radiation.³ So far very little use has been made of the alpha rays in therapy. It is probable, however, that in the future a way will be found to utilize the large amount of energy carried by the alpha particles. In this case the use of emanation offers greater possibilities.

In another paper will be taken up the direct applications of radioactivity to therapy, with special reference to the effects on dosage of filtration, distance and absorption of the radiations in tissue.

3. An account of the present uses of radium emanation will be found in an article on "Radium Technique at the Memorial Hospital, New York," by G. Failla, *Arch. Radiol. & Electroth.* **25**:3 (June) 1920.

DIGESTION OF KELOIDS, CICATRICES AND BUBOES WITH PEPSIN-HYDROCHLORIC ACID

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The latest histologic experiments of Unna have proved that the digestive power of pepsin and hydrochloric acid combined penetrates the horny layer of the epidermis and that this combination may even be used for carrying other chemical agents through the horny layer. A large number of chemicals can thus be caused to be absorbed by the surface of the skin; this has hitherto been impossible to accomplish, as, for instance, in the case of epinephrin. Naturally, in the first place it is the pepsin and hydrochloric acid itself which penetrate the intact horny layer. When this combination has penetrated to a certain depth it will affect certain diseases of the cutis and subcutis, as I shall try to show.

Our experiments were first tried on keloids and scarring after burns, cicatrices, with the intention of testing the possibility of digesting the fibrous (collagenous) tissue, of which these scars chiefly consist. The following solution was used: pepsin, 10 c.c.; muriatic acid, 1 c.c.; phenol, 1 c.c. Distilled water to make 200 c.c. was added. Phenol was added in order to prevent possible putrefaction of the decaying tissue.

The hydrochloric acid necessary for the digesting effect of pepsin has in itself some antiseptic property. We prefer, however, to add the same quantity of phenol, which in no way hinders digestion, but has the advantage of preventing the slightest degree of putrefaction. At the same time, phenol represents a useful antipruritic in many skin diseases. Compresses of absorbent cotton soaked in the above mentioned solution were applied and then covered with an impermeable cover in a large number of cases.

The cosmetic effect on scarring after burns was excellent. In many cases of fresh scars no trace was left after a systematic application of our digesting method. These successes led to the local treatment of *ulcus durum*, the latter being a reaction of the system against *Spirochaeta pallida*, chiefly by hypertrophy of the fibrous tissue, first surrounding the blood vessels.

The induration was digested by similar compresses with pepsin-hydrochloric acid, with impermeable covering. Though the excision of the ulcer in this condition must be acknowledged as the quicker and more radical method, there are cases in which after a thorough arsen-

amin treatment the initial sclerosis has healed perfectly, yet a certain obstinate hardness remains, which will not give way to the strongest antisyphilitic treatment. Our pepsin compresses showed excellent success in those very obstinate cases in which the labia majora are changed into broad and hard masses of tissue.

From the same point of view we treated cases of adenitis caused by different infections, such as buboes following soft chancre. Almost every patient we treated showed a regression of the inflammation within from two to three weeks without an incision being necessary. In one case of bubo on both sides we made an incision in the left side, and injected iodoform glycerin, while we treated the right side with pepsin-hydrochloric acid compresses. The latter was completely absorbed before the wound on the left side had healed. The effect of pepsin-hydrochloric acid on infected glands in these cases can only be explained by the bactericidal power of phenol plus hydrochloric acid besides the digestion of the inflamed tissues by pepsin.

TREATMENT OF TUBERCULOUS GLANDS IN CHILDREN

We then took up the general treatment of all masses and packets of tuberculous glands in children, especially those of the throat and neck. In these cases, pepsin compresses represent a good substitute for surgical treatment, the more so as the incision of tuberculous glands is not in all cases free from risk, since more than one case of lupus has had its origin in this procedure.

XVIII.—(A) VON RECKLINGHAUSEN'S DISEASE IN
THE NEGRO; (B) CURVATURE OF THE
SPINE IN VON RECKLINGHAUSEN'S
DISEASE *

RICHARD S. WEISS, M.D.

ST. LOUIS

A. VON RECKLINGHAUSEN'S DISEASE IN THE NEGRO

Von Recklinghausen's disease, fibroma molluscum, in the negro race is undoubtedly extremely rare. I have been unable to find any case reports in the literature and can find no reference to this condition in the negroes in the many textbooks consulted. Howard Fox (personal letter, 1917) states that he has no reference to this condition, and H. H. Hazen (personal letter, 1917) states that he has never seen such a case, although one occurred in his service during his absence, in the person of a young negro woman. Both of these observers have an extremely large negro service. I have gone over the recent literature concerning skin diseases in the army and can find no reference there to this condition in the negro. Hutchins¹ observed three patients with von Recklinghausen's disease who were admitted to his service in the base hospital at Camp Pike, Ark., but he does not state whether they were negroes or white men. Hazen,² in an analysis of 1800 cases of skin disease seen by him as a member of a medical advisory board, states that 1,384 of the patients were white and among these white men, one case of von Recklinghausen's disease was observed. Four hundred and sixteen patients were negroes, and no case of this disease was noted.

The two cases herein reported are the only ones that have been observed in the service of Drs. Engman and Mook, which includes a large number of negro cases.

REPORT OF CASES

CASE 1.—*History*.—M. L., a negress, aged 22, entered the Dermatological Clinic of the Washington University Dispensary on Feb. 15, 1916, complaining of an eruption on the body. The patient was born in Missouri, was married

* Studies, reports and observations from the Dermatological Departments of the Barnard Free Skin and Cancer Hospital and the School of Medicine, Washington University, St. Louis, Mo., U. S. A., service of Drs. M. F. Engman and W. H. Mook.

1. Hutchins: Skin Diseases at an Army Camp, *J. Cutan. Dis.* **37**:456 (July) 1919.

2. Hazen: Dermatology and Syphilology in a Medical Advisory Board, *J. Cutan. Dis.* **37**:779 (Dec.) 1919.



Fig. 1 (Case 1).—Von Recklinghausen's disease in a negress, showing pigment spots and peculiar serrated tumor.

and was a housewife. Her father, 52 years old, and her mother, 50 years old, were both in good health. She had three brothers aged 20, 18 and 15, and two sisters, aged 27 and 26; all were in good health. Three brothers were dead: two died in infancy and one at the age of 25 of pulmonary tuberculosis. There was no further history of tuberculosis and no history of cancer, skin diseases, nervous or mental disturbances. The patient stated that to her knowledge no one in the family ever had any skin condition resembling hers.

She had varicella and measles in childhood. She never had had any serious illness since. There was no history of syphilis or gonorrhea. Menstruation began at the age of 15. It had always been regular and without pain until about March, 1915. It then became irregular to such an extent that the patient never knew when to expect the flow. It lasted from four to five days; the flow was scanty; there was no pain. She had been married three years. Her husband was apparently in good health. She had no children. She had had one miscarriage. She slept well and ate her meals regularly. She drank beer moderately and coffee once daily. Her bowels were constipated. Her appetite was good.

Present Trouble.—This was first noticed at the age of 12. It began as "small lumps in the skin" which gradually became larger. The spots on the skin were noticed a little later.

Examination.—The patient gave facts and dates inexactly. Her responses were slow. Mentality was apparently very low. The pupils were equal and reacted normally to light and accommodation. The cranial nerves were negative. The heart and lungs were apparently normal. The abdomen and extremities were negative. The reflexes were normal. The Wassermann test and the tests of the urine were negative.

The Skin.—The skin presented three types of lesions.

Type 1: Pigmented areas, of a dark brown color, varying in size from a pinhead to a quarter. They were thickly scattered over the chest, shoulders and upper portion of the back and sparsely on the abdomen and lower part of the back.

Type 2: Small pendulous tumors, not more than twenty in number, on the back, chest and arms. These tumors were soft and the skin covering them was thin and wrinkled. Several could be pushed back into the subcutaneous tissue as if through a hernia opening. There was a pendulous, empty sack of skin, about the size of a filbert, in the center of the pubic region.

Type 3: There were several large, flat, boggy tumors, covered with peculiar serrated and pigmented skin (Fig. 1). The largest of these, about 6 by 8 cm., was on the left side of the back just below the scapula. Another one, 1 by 2 cm., was over the left greater trochanter. A third of about the same size appeared on the flexor surface of the right knee. The fourth, about 0.5 cm. in diameter, was seen on the anterior surface of the thorax, just above the left breast.

A small pendulous tumor was removed at biopsy from the back without the use of anesthesia and placed in a 10 per cent. formaldehyd solution. A frozen section was made and stained with hematoxylin-eosin. The pathologist called the condition fibroma (Dr. George Ives).

CASE 2.—*History.*—H. W., a negro, aged 46 (?); born in America, was admitted to the Barnard Free Skin and Cancer Hospital, Aug. 19, 1916. His condition was diagnosed as fibroma molluscum. The family history was not known to the patient; he did not know of any relatives that had a similar disease. He had never been seriously ill. As a child, he had noticed many



Fig. 2 (Case 2).—Von Recklinghausen's disease in a negro.



Fig. 3 (Case 2).—Von Recklinghausen's disease in a negro.

small tumors in the skin. These had increased in size, and in the course of years many new tumors had developed. Several years ago a large, irregular, soft mass developed in the right thigh; it became so large that the thigh became pendulous and caused a great deal of inconvenience.

Physical Examination.—The patient was a poorly developed, somewhat emaciated negro who looked as though he were about 50 years old. Examination of the heart and lungs revealed no gross abnormalities. There was some tenderness over the gallbladder. The patient's mentality was distinctly below normal, but there were no signs of gross central lesions. Urine examination revealed nothing abnormal. The blood pressure was systolic, 108; diastolic, 60.



Fig. 4 (Case 2).—Von Recklinghausen's disease in a negro.

The Skin.—The skin of the entire body presented a remarkable picture. Scattered over its entire surface were tumors varying in size from 2 or 3 mm. to large irregular and lobulated masses, 20 to 25 cm. in length and as great or greater in breadth. The face and scalp showed numerous lesions. The trunk was studded with them, particularly the back. There were numerous lesions on the arms and hands. On the thighs and legs, the smaller definite tumors were sparse, but the right thigh and knee were covered with large, boggy, lobulated masses. The condition can best be studied from the illustrations (Figs. 2, 3, 4 and 5). The masses on the thigh interfered with the return flow of the blood

and probably the lymph, so that the swelling of the leg was probably a combination of edema and lymph stasis.

Some of the tumors were pedunculated. Others were apparently empty sacs of skin, the contained tumor having disappeared. Some of the smallest growths could be pushed back into the skin through hernia-like openings. Few pigmentary changes could be observed. The skin covering a few of the moderate sized tumors was decidedly darker than the normal skin. There were no small pigmented spots.



Fig. 5 (Case 2).—Von Recklinghausen's disease in a negro.

There was a moderate right lateral curvature of the spine in the dorsal region.

B. CURVATURE OF THE SPINE IN VON RECKLINGHAUSEN'S DISEASE

A point in connection with von Recklinghausen's disease that we have been unable to find in the literature has been called to my atten-

tion by Dr. Engman. He says that in every case of this disease that has come under his observation, lateral curvature of the spine was noted. Since 1913, this symptom was found in the fifteen cases that have appeared at the Barnard Free Skin and Cancer Hospital and the Washington University Dispensary. An interesting private case of Dr. Engman's may be cited.

History.—Miss Z., a child of 15 years, was seen at the office April 25, 1916. The mother said that the patient had had no serious illness up to 1913, when she became nervous and was "threatened with St. Vitus dance." She began to menstruate in November, 1915, but had not been regular since that time. There was no history of a similar skin disease in the family.

At the age of 4 months, a pigmented patch was noted on the left hip. A few more spots appeared during infancy and infrequently more appeared until the last year or so, when they began coming out more rapidly. In 1914, a reddish tumor appeared on the arm. Since the beginning of menstruation, tumors had appeared all over the body, some on the skin and some subcutaneously.

Physical Examination.—The patient had a peculiar facies, that of a woman of 25. She was below the average height, but was well developed and well nourished. On examining her stripped, it was found that her appearance was that of a woman of 25 or 30. The figure was that of a woman of that age, the hips prominently curved, shoulders slightly stooped, arms and shoulders well developed. The breasts sagged and were not hemispherical. There was a moderate lateral curvature of the spine.

Scattered over the skin were splashes of café au lait pigment of various sizes. They ranged from a small dot to streaks in the cleavage line of the skin. Some of them were 4 inches long and 2 inches wide in the center, tapering off at the ends. There was an attempt at symmetry but symmetry was not exact. Scattered over the arms, legs and body were about fifty small fibromas, some deep in the skin and some more superficial. The skin over a few was normal in color, but over the majority it was purplish-red. The tumors varied in size from 2 to 5 mm.

This case is a rather curious type—a prematurely developed child of 15, with the appearance, build and figure of a woman of 25 or 30, and having a slight lateral curvature of the spine and possibly an anteroposterior curvature also. These facts taken together with the abnormality in menstruation might suggest an endocrine origin.

COMMENT

Naturally one is unable to state without further investigation, the relationship of this curvature to von Recklinghausen's disease. I merely wish to call attention to this observation, as its constant occurrence appears to be of some clinical significance. It seems to be a part of the syndrome in this peculiar disease.

FIBROMYXOMA—PROBABLY A LINEAR NEVUS

REPORT OF A CASE *

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The following case is reported as one that is apparently unique in medical annals. A careful search of the literature on nevus at the Library of the Army Medical Museum did not reveal a case in which myxomatous tissue had been found. The literature on myxoma and fibromyxoma is scant. No clue to a tumor of similar distribution can be found in textbooks or in current literature.

CASE REPORT

History.—E. D., a colored woman, aged 33, married; a laundress, gave an unsatisfactory family history. Her past history was negative. She had had no previous skin disease and no other serious illness. She had had no children. Her present illness began at birth.

Examination.—The condition was located on the left arm, beginning about 3 inches below the axilla and extending to the center of the palm. On the under surface of the arm, as it was extended with the hand midway between pronation and supination, there was a pendulous, lobulated mass of doughy consistency. In size the tumor was about half the thickness of the normal arm, giving the diseased arm the appearance of being twice the normal size. The skin over the tumor was more deeply pigmented than the normal skin of the patient. Above the tumor, and in a line with it, was a typical pigmented nevus (which does not show in the illustration), about 5 cm. long and 3 cm. wide. The consistency and appearance caused us to make a diagnosis of linear fatty nevus at the time of the first examination. Biopsy was performed at once. The pathologists of the Army Medical Museum reported the tissue a fibromyxoma with no fat tissue present.

Differential Diagnosis.—This tumor was classified as a nevus for several reasons. The history showed that the condition was present at birth and had remained essentially unchanged ever since. There had been no subjective symptoms except the annoyance of the increased size and consequent clumsiness of the affected arm. The color of the skin was darker than normal, showing pigmentation in the affected area. There was an undoubted pigmented nevus just above the tumor, in a line with it, and of the same depth of color. The distribution of the lesion was that common for linear nevi, and followed closely the cutaneous distribution of the first dorsal nerve root. Furthermore, since nevi are probably all congenitally misplaced or maldeveloped tissue, it is no stretch of the imagination to suppose that the present tumor was the result of the failure of the embryonic myxomatous tissue to develop into connective tissue, which it ultimately becomes in the course of development.

* From Freedmen's Hospital Skin Clinic, service of Dr. H. H. Hazen.



Fig. 1.—Lesion on arm of patient. Keloid at site of operation is well shown. Sensation over the growth was normal.



Fig. 2.—Fibromyxomatous tissue, low power. The fibromyxomatous tissue involves and takes the place of the corium and subcutis. The tumor is therefore not a myxomatous degeneration of the fascia, but a true cutaneous tumor. This and the following photomicrograph were made by the pathologist of the Army Medical Museum.

Among other conditions considered, but not fitting the case, were von Recklinghausen's disease and a malformation as a result of intra-uterine adhesion. It was improbable that the condition was von Recklinghausen's disease as there were no other tumors on the body, no other pigmented spots, and no nerve tissue was found in the section. It was unlikely that this was a case of intra-uterine adhesion as in the normal fetal attitude the lesion as presented would necessarily have been placed against the patient's abdomen, in part at least, and there would have been evidence of the adhesion there as well as on the arm. Injury at the time of delivery could not be excluded, as we had no history on this point. Either of these conditions, however, would be much

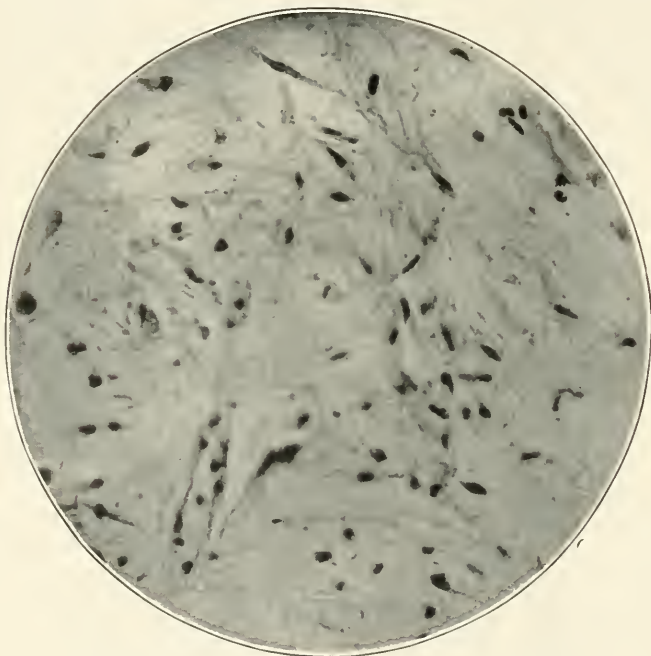


Fig. 3.—Fibromyxomatous tissue; high power.

more apt to have resulted in scar formation, and later contracture and keloid than in tumor formation of the type present. That there was a strong tendency to keloid formation in the patient was shown by the presence of this condition in the site of the incision made to remove the tumor some months before our examination.

Treatment.—Owing to the previous failure of surgery, the patient would not consent to further operative interference. No other treatment seemed to offer any hope of success.

The author wishes to express his appreciation to Dr. Hazen for permission to publish the case and for his kindly advice and criticism.

A CASE OF MULTIPLE IDIOPATHIC HEMORRHAGIC SARCOMA (KAPOSI)

KENDAL P. FROST, M.D.

LOS ANGELES

REPORT OF CASE

History.—The subject of this report first came under observation in January, 1919. He was an Austrian Jew, 48 years of age. He complained of pain and swelling in the legs and arms and a cutaneous disorder of about fifteen months' duration. The lesions appeared first on the hands, later on the legs. The toes, ears and body finally became affected. The lesions were accompanied by swelling of the hands and feet. At the time of the first examination the lesions were large and numerous on both hands and feet. Scattered lesions were present on the arms, legs and trunk. There was one lesion on the right eyebrow and one on each ear. The patient stated that the lesions began as hard, flat, elevated red areas about the size of peas. They gradually grew larger and those on the hands and feet in some instances coalesced to form plaques. Previous to the onset of the skin manifestation he noticed itching of the ears and back. This was not present at the time of examination, there being no subjective sensations except pain in the swollen lower extremities. For about six months he had noticed an enlargement on the left side of the chest which had slowly increased in size to about that of a hen's egg. It was not painful nor in any way disturbing except on account of its size and location. The patient had always been well except for an attack of pneumonia some years ago. He had had no previous skin disorder nor was there anything in his family history bearing on his present condition.

Physical Examination.—The patient was a well developed, rather stout, middle aged man. His general condition was good. Scattered diffusely over the body, being more profuse, however, on the hands, feet and lower portion of the back, were dull red to brownish, infiltrated, flat nodules from the size of a pea to that of a quarter dollar. The smaller lesions were more erythematous than the larger ones and those on the extremities were distinctly purplish. Many of the larger lesions were less infiltrated, and there was less discoloration and infiltration in the center of the plaques. On the hands and feet the lesions had become confluent, forming large, purplish, infiltrated plaques; on each ear, involving chiefly the central portion, was a purplish, infiltrated plaque gradually fading at the border into the normal skin. The lesions on the body elsewhere were sharply demarcated from the surrounding normal integument. The nodules were all fixed to the skin and apparently extended into the deeper layers of the corium. In the left anterior axillary line under the lateral border of the pectoralis major muscle was an egg-sized, hard mass which was freely movable and apparently not fixed to the surrounding structures. In the supraclavicular space on each side was a similar but smaller nodule. There was considerable brawny edema of the legs, extending almost as high as the knees, and of the hands and lower forearms. There were no lesions in the mouth or pharynx. No changes in the viscera were discernible by ordinary examination. The urine was negative, and there were no changes in the blood. There was 80 per cent. of hemoglobin. Leukocytes and erythrocytes



Fig. 1.—Full length view of the patient showing general distribution of the lesions.



Fig. 2.—Types of lesions on the legs when the patient first came under observation.

were present in normal numbers, and a differential count of the leukocytes revealed no disturbance in the proportions of the various elements. A biopsy was performed August, 1919, a lesion on the inside of the right thigh being removed at that time. The second biopsy was performed August, 1920, a lesion over the sacrum being removed.

The treatment consisted of arsenic used internally and roentgen-ray therapy. There was considerable improvement, especially after radiotherapy was begun. The lesions, especially those on the hands, became much less infiltrated. The edema and pain in the legs decreased greatly. The lesions on the ankles and on the calves and sides of the legs became cystic. This change began to occur



Fig. 3.—Lower portion of the leg showing beginning cystic change.

in July, 1920, when a few cysts the size of a split pea appeared in the regressing lesions. These cysts increased in number and size until at the time of writing they were scattered over the lower two thirds of the leg below the knee and ranged in size from that of a pea to that of a small cherry. This change was probably due to static conditions. There was no pain except in the right great toe on which there was a vascular sessile tumor, the size of a pea, which was surrounded and covered by a warty keratosis. This lesion improved considerably under radiotherapy.

Histopathology.—The tissues removed at biopsy were fixed in Zenker's fluid and stained in several different ways. In general, there was a slight atrophy of the stratum corneum, and the papillary processes were slightly shortened. There was slight edema. In the corium groups of cells appeared. In most of the sections this cell infiltration lay deep, but in a few places there was a rather diffuse cellular growth in the superficial portions. The cellular infiltrations in some places were around hair follicles and coil glands, and in practically all instances there was an increase of the vascular elements in the cell mass. Except in the portions where the growth was in the superficial layers, it was well demarcated from the surrounding connective tissue, but there was no definite capsule. Collagen fibers did not penetrate the cell group.

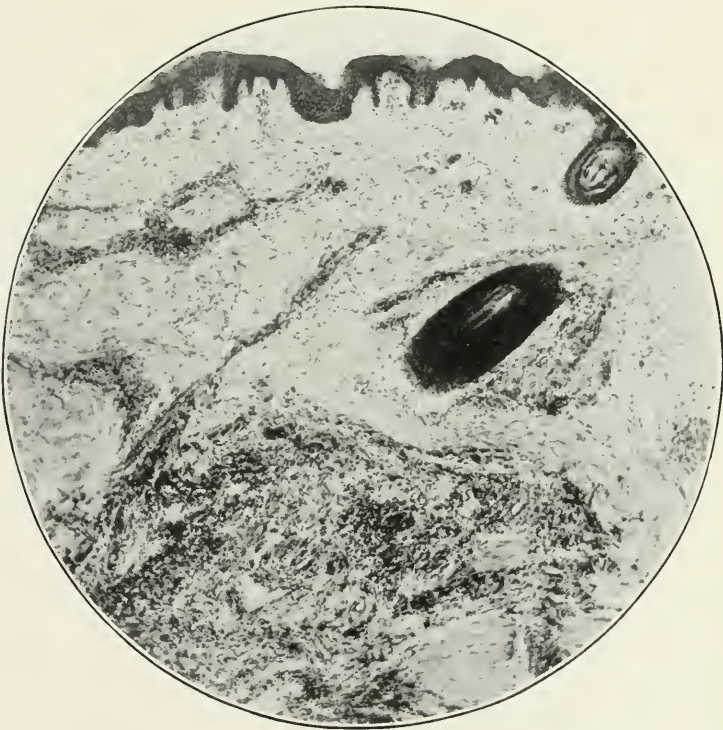


Fig. 4.—Photomicrograph showing the general distribution of the cell infiltration; $\times 60$.

Along the course of the blood vessels elastic fibers were seen to pass into the cell mass. The cellular elements were of several types; round and spindle shaped cells predominated. In some parts, areas of a single type of cell were seen. In most places there was a mixture of round and spindle cells and cells with irregularly shaped nuclei. There were a few scattered mast and plasma cells. In the peripheral portions of the cell masses there were large deposits of yellowish brown pigment which was largely intracellular and granular. The granules were fairly uniform in size and were usually round. There was some extracellular pigment but not a large amount.

The vascular elements were proliferated, there being apparently many more vessels and capillaries than were seen in a normal tissue. The capillaries and lymph spaces were dilated. In practically all parts of the sections the vessels were empty. In a few places there was a slight proliferation of the endothelium, but in most parts there was apparently no change. No hemorrhages were to be seen in any part of the sections.

In sections from a second biopsy the general structure of the tissue was the same. The cellular elements were scant, however, and there was no pigment. The vascular proliferation and dilatation persisted.

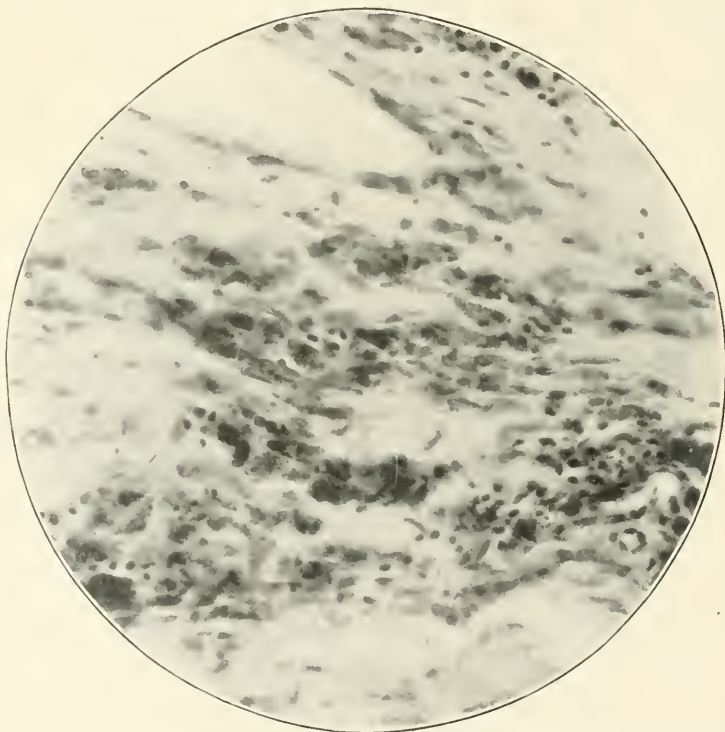


Fig. 5.—Photomicrograph showing types of cells and vascular proliferation; $\times 325$.

This case corresponds clinically to the cases described first by Kaposi under the title of "Multiple Idiopathic Hemorrhagic Sarcoma." Since the publication of his report, numerous cases have been reported and various interpretations have been given to the histology. Some authors hold that it is a true sarcoma, while others incline to the view that it is primarily a granuloma and may later become neoplastic. Sellei¹ strongly advocates the view that it is a granuloma. Pollitzer² con-

1. Sellei: *Monatsh. f. prakt. Dermat.* **34**:497, 1902.

2. Pollitzer: *J. Cutan. Dis.* **27**:143, 1909.

siders it a true sarcoma. Sequeira believes it to be an inflammatory condition. Gilchrist and Ketron³ report two cases in which the histologic picture varies from that of an angioma to that of a type of tissue resembling a connective tissue new growth. Ewing⁴ states that it is "an infection granuloma of unknown origin which in its later stages in predisposed subjects and under suitable conditions may take on genuine neoplastic properties. . . . The entire vascular system seems to be overtaken by degeneration with overgrowth of vaso-for-

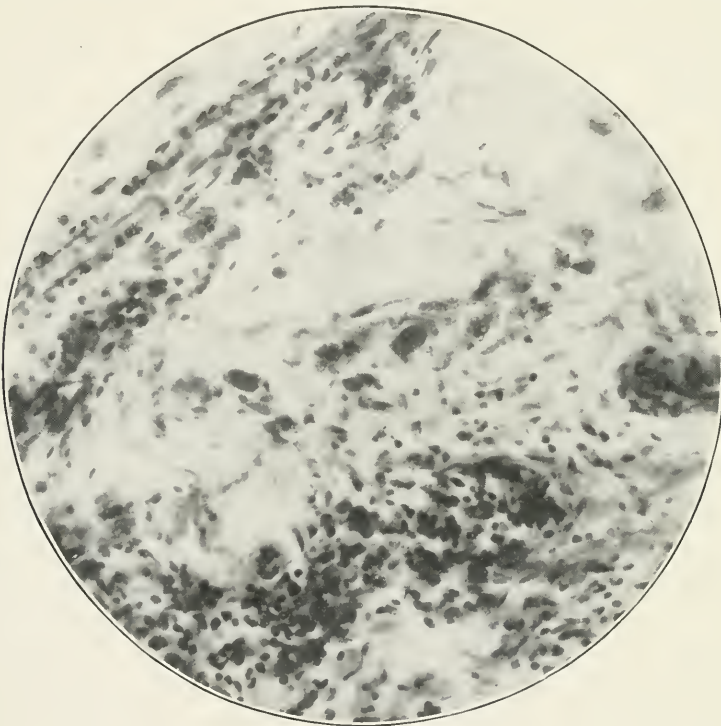


Fig. 6.—Photomicrograph showing types of cells and vascular proliferation, with a group of pigment cells in the center of the field; $\times 325$.

mative cells, leading in many instances to true tumor formation." Justus⁵ reports inoculating white mice with tissue from a case of multiple idiopathic hemorrhagic sarcoma (Kaposi) with production of systemic lesions. He carried the condition through five generations of mice.

It is difficult to draw conclusions from a single case, yet the diffuse

3. Gilchrist and Ketron: *J. Cutan. Dis.* **34**:429, 1916.

4. Ewing: *Neoplastic Diseases*, Philadelphia, W. B. Saunders Company, 1919.

5. Justus: *Arch. f. Dermat. u. Syph.* **99**:446, 1910.

nature of the growth with the multiplicity of cell types, and close relation of the cell masses to epithelial structures and blood vessels, tends to a view that the lesions in this case have been produced on an inflammatory basis. The cells themselves are, however, largely connective tissue types, and there is a practical absence of the cells usually found in active inflammatory processes.⁶

I wish to express my thanks to Dr. Oliver S. Ormsby for providing the material for this study, and to him and Dr. H. Gideon Wells for many helpful suggestions in the interpretations of the histopathology.

6. In addition to the references already given, the following articles may be of interest:

Macleod: *Brit. J. Dermat.* **17**:173, 1905.

Mariani: *Arch. f. Dermat. u. Syph.* **98**:267, 1909.

Correspondence

"SO-CALLED DERMATITIS DYSMENORRHEICA"

To the Editor:—In our paper on "So-Called Dermatitis Dysmenorrheica," which appeared in the December, 1920, issue, page 725, we omitted to note the following additional references to the literature.

1. Kreibich: Arch. f. Dermat. u. Syph. **114**:161, 1913.
2. Friedeberg: Ibid., p. 173.
3. Mathes: Ibid., p. 185.
4. Matzenauer and Polland: Ibid. **116**:185, 1913.
5. Rasch: Ibid. **121**:21, 1915.
6. Brauer: Ibid. **124**:595, 1918.

FRED WISE, M.D., AND H. J. PARKHURST, M.D., New York.

News and Comment

MODELS OF SKIN DISEASES

Dr. J. Frank Wallis has announced the establishment of a Laboratory of Medical Art at 1752-1754 S Street N.-W., Washington, D. C., to furnish moulages of skin diseases and syphilis. For two years, while in the army, Dr. Wallis has been making these moulages for the Army Medical Museum, and has been doing work of a high quality. It will be a great advantage to be able to secure such models. Their value was established by the Barretta Museum in Paris a long time ago.

Dr. Wallis is prepared to furnish models from his own collection or to make them from material submitted by physicians.

Abstracts from Current Literature

STUDIES IN THE STANDARDIZATION OF THE WASSERMANN REACTION. XII. THE TITRATION OF HEMOLYSIN AND SENSITIZED VERSUS PLAIN RED BLOOD CORPUSCLES IN COMPLEMENT-FIXATION TESTS. JOHN A. KOLMER, ANNA M. RULE and MARY E. TRIST, *Am. J. Syph.* 4:616 (Oct.) 1920.

The authors' summary and conclusions are:

1. In the titration of hemolysin the unit or measure of activity varies greatly according to the amount of complement used, the amount of natural hemolysin in the complement, the kind and duration of incubation and, to some extent, according to the manner of mixing hemolysin, cells and complement.

2. The proper amount of complement to employ for the titration of hemolysin is the average amount found best by experience as the unit for conducting the complement-fixation test.

3. The use of a mixture of guinea-pig serums for complement is generally a satisfactory adjustment for the natural hemolysin present, especially if the hemolysin is titrated daily before the titration of complement.

4. An incubation of one hour in a water-bath at 38 C. is generally satisfactory for determining the unit of hemolysin; one-half hour is too brief and over one hour unnecessarily long, as the absolute end point of hemolysis is not required.

5. In setting up the hemolysin titration the cells and hemolysin should not be left in contact before the addition of complement, because irregular sensitization of the cells may occur; in practice it appears best to pipet the complement followed by the corpuscles and lastly by the hemolysin and saline solution.

6. Sensitization of corpuscles is best accomplished by mixing corpuscles and hemolysin at ordinary room temperature for one hour.

7. While sheep corpuscles may absorb twelve or more units of hemolysin, the absorption of more than from four to six units does not increase their susceptibility to the hemolytic activity of complement.

8. Sensitized corpuscles are more susceptible to the hemolytic activity of complement than plain corpuscles in the presence of the same amount of hemolysin; therefore in complement-fixation tests, if any complement remains unfixed by syphilis antibody and the extract, the degree of hemolysis will be greater when sensitized corpuscles are added and the reactions consequently less sensitive than when plain corpuscles and hemolysin are added separately. This explains the following:

(a) In complement-fixation tests conducted with an arbitrary and fixed amount of complement as in Wassermann's method, the use of corpuscles sensitized with two units of hemolysin yielded less sensitive reactions than tests in which the plain corpuscles and hemolysin were added separately.

(b) When complement was titrated with plain corpuscles and two units used in comparative complement-fixation tests with plain and sensitized corpuscles, the tests with sensitized corpuscles generally yielded less sensitive reactions.

(c) When comparative complement-fixation tests were conducted with two units of complement titrated with plain corpuscles and two units titrated with the sensitized corpuscles, the reactions were more nearly equal in sensitiveness,

although the tests with plain corpuscles were generally more sensitive. Under these conditions the unit of complement with sensitized corpuscles was less than with plain corpuscles and consequently the reactions with sensitized corpuscles were rendered more delicate than those in which sensitized corpuscles were used with a constant arbitrary amount of complement as in *a*, or with complement titrated with plain corpuscles as in *b*.

8. Corpuscles sensitized with from four to six units of hemolysin are not susceptible to the influence of natural hemolysins in complement and patients' serums, and if sensitized corpuscles are employed in the conduct of complement-fixation tests, it would appear advisable to sensitize with five units of hemolysin rather than with two units, as is the usual custom.

10. Sensitized human corpuscles could not be used because of the occurrence of agglutination with the majority of rabbit antihuman hemolytic serums.

11. Demonstrable dissociation of hemolysin from corpuscles was not found unless the cells were sensitized with six or more units of hemolysin; under these conditions dissociation was evident within half an hour. Accordingly, dissociation of hemolysin does not constitute a contraindication to the use of sensitized corpuscles.

12. The principles of a standardized technic for the titration of hemolysin are given; the details of the titration and the amount of hemolysin recommended for the conduct of a standardized complement-fixation technic, will be published later.

STUDIES IN THE STANDARDIZATION OF THE WASSERMANN REACTION. XIII. THE INFLUENCE OF HEATING SERUM UPON COMPLEMENT FIXATION IN SYPHILIS. JOHN A. KOLMER, ANNA M. RULE and MARY E. TRIST, *Am. J. Syph.* **4**:641 (Oct.) 1920.

The authors' conclusions are:

1. Although heating syphilitic serums results in the destruction of a portion of the antibody concerned in the complement-fixation test, it is advisable to heat all serums for the purpose of inactivating native complement and thereby permitting a closer adjustment of the hemolytic system, destroying any anti-lysins (anticomplementary substances) that may be present, and preventing the occurrence of pseudo-positive or proteotrophic reactions with the serums of nonsyphilitic persons.

2. For these purposes heating serums at 55 C. for fifteen minutes is sufficient and preferable to the customary period of thirty minutes, as less destruction of antibody occurs.

3. The inevitable reduction in the sensitiveness of complement-fixation tests conducted with heat serums should be compensated for in a standardized technic by certain technical procedures and particularly with reference to the kind and amount of antigen employed and the adjustment of the hemolytic system.

STUDIES IN THE STANDARDIZATION OF THE WASSERMANN REACTION. XIV. THE INFLUENCE OF TEMPERATURE AND DURATION OF PRIMARY INCUBATION UPON THE HEMOLYTIC ACTIVITY OF COMPLEMENT. JOHN A. KOLMER and ANNA M. RULE, *Am. J. Syph.* **4**:675 (Oct.) 1920.

The authors' conclusions are:

1. The hemolytic activity of guinea-pig complement is reduced by primary incubation at 38 C., especially in a water-bath for one hour; this partly explains

the stronger Wassermann reactions observed after a primary incubation of one hour in a water-bath, as compared with one hour in an incubator.

2. The hemolytic activity of complement is slightly reduced by primary incubation at from 2 to 8 C. for from four to eighteen hours, but is markedly reduced under these conditions when titrated in the presence of antigen.

3. When complement-fixation tests in syphilis are conducted with a primary incubation of from four to eighteen hours at from 2 to 10 C., with or without an additional incubation of one-half to one hour at 38 C., stronger reactions may be expected with some serums, due in part to the greater destruction of complement and consequent closer adjustment of the hemolytic system under these conditions than occurs during the usual primary incubation of one hour at 38 C.

TOMLINSON, Omaha.

THE TREATMENT OF LEPROSY. SIR LEONARD ROGERS, *Indian Med. Gaz.* 55:125 (April) 1920.

Rogers reports the progress made by patients previously treated and reported by him in the *Indian Journal of Medical Research* of October, 1917, and fourteen more cases reported in the *Indian Medical Gazette* of May and June, 1919; he also reports eleven more recent cases, making a total of fifty-one cases.

The results may be summarized as follows: One complete failure of the treatment; nine patients whose condition was slightly improved, in only one of whom the treatment was continued for over a year; twenty patients much improved, in only two of whom treatment was continued over one year; and twenty-one, or over 40 per cent., in whom the lesions disappeared completely. Nine of the latter patients were treated about a year. Rogers believes that the duration of the treatment is a most important factor.

Rogers tabulates the after-results of the cases followed up, including twenty-six of the forty cases in the first two series reported. The more recent eleven cases are not included, being too recent for this purpose:

	Sodium Hydnocarpate	Sodium Morrhuate
Total cases	40	14
Not followed up.....	14	6
Followed up	26	8
Not improved	1	..
Further improved	5	5
Lesions disappeared	5	..
Remaining well	10	3
Relapsed	5	..

Summary of Results Obtained with Sodium Morrhuate.—In 1919 fourteen patients were treated and six more have been treated since, making a total number of twenty cases, as tabulated above. No patient was treated for over one year and only six longer than six months, yet twelve showed much improvement and the lesions disappeared in five, including a negative bacteriologic examination. On the other hand, three patients treated for only four or five months showed slight improvement. The three patients in whom the lesions disappeared last year still remain well.

This preparation is borne much better than hydnocarpate. It is painless given subcutaneously, and when given intravenously does not cause thrombosis of the veins.

Results of Further Researches.—Rogers discovered that the acid-fast destroying property of derivatives from chaulmoogra oils was not specific to that group, but was also possessed by products such as cod-liver oil. This property seems to reside in the fatty acids as a class. The sodium salts of the unsaturated fatty acids of linseed and soya bean oils were therefore tried. The former seemed to be irritating when given subcutaneously, and when given intravenously it did not yield any promising reactions. The sodium salt from soya bean oil proved to be less irritating to the subcutaneous tissues and to the veins than the hydnocarpates, while it gave well marked local reactions to leprotic tissues in the usual therapeutic doses. In one case it has proved effective, while in the other cases it did not seem to give as good result. Rogers believes that further experience may give better results.

Ethyl esters of unsaturated fatty acids were also tried, particularly ethyl esters of chaulmoogra acid, but these were found to be too irritating to the tissues, and produced no good effects in the few injections tried. Rogers therefore tried to prepare a similar product from cod-liver oil, which he calls ethyl morrhuate. He has given it in both leprosy and tuberculosis by the subcutaneous method with very little trouble to the patient and with distinctly favorable results. This preparation was also tried intravenously in rabbits and was found to be innocuous.

GUTIERREZ, Manila,

CURSO DE DERMATOLOGIA Y SIFILOGRAFIA, HOSPITAL DE SAN LUIS (COURSE IN DERMATOLOGY AND SYPHILOLOGY, SAINT LOUIS HOSPITAL, PARIS). Informacion General, Los Prog. de la Clin. 8: (Sept.) 1920.

Los Progresos de la Clinica has arranged a course at the Saint Louis Hospital for visiting Spanish physicians. It seems worthy of interest to outline the course.

DERMATOLOGY

Dermatologic prescriptions	Rules for treatment of eczema. Pathogenesis of eczema and dermatitis
Local treatment	New treatment of psoriasis
External treatment of eczema	Treatment of pruritus, lichen and lichenification
Treatment of alopecia and nevi	Treatment of seborrhea and acne
Exfoliative dermatitis and glandular alterations; phototherapy in dermatology	New treatment of pyoderma
Cutaneous complications of wounds, pyoderma, tuberculosis and post-traumatic syphilis	Treatment of streptococcic dermatitis
Vaccines; preparation and injection	Treatment of cutaneous gangrene, of leg ulcers, and elephantiasis
New treatment of scabies and pediculosis; disinfection	Treatment of lupus
Scarification and caustics	Finsen therapy
Treatment of lupus erythematosus, carbon dioxide snow, etc.	New data concerning the tuberculids, sarcoids, etc.
Tuberculin therapy	New treatment of leprosy
Mycoses, sporothricoses, etc.; diagnosis by culture; treatment	Tinea; diagnosis and roentgen-ray therapy
Diagnosis of tumors by biopsy	Phenomena of shock in dermatology. Sensitization. Vaccination and auto-hemotherapy
Treatment of epithelioma by roentgen ray	Prophylaxis of cutaneous cancer; pre-cancerous stages; false cancer
Treatment of ichthyosis, pigmentation and keloids	Treatment of hypertrichosis; electrolysis

SYPHILOLOGY

Status of arsenotherapy	Treatment of secondary, tertiary and malignant syphilis
New mercurial compounds; iodids	Prophylaxis of nervous syphilis
Treatment of the primary lesion.	New data concerning tabes and paresis. The duality of the cause
Data concerning the evolution of the primary stage. Retarded syphilis	The Wassermann reaction
Diagnosis of syphilitic chancre and mixed sore	Status of venereal prophylaxis
Stain of Fontana-Tribondeau	Caution and treatment of latent secondary syphilis
Intravenous and intramuscular injection of arsenicals	Lumbar puncture, cell count, albumin determination
Reactions to arsenicals	Treatment and feeding of heredosyphilitics
Soft chancre and its adenitis	The Wassermann reaction and treatment
Ultramicroscopy	

GOODMAN, New York.

THE MANCHESTER AND DISTRICT RADIUM INSTITUTE, THE ROYAL INFIRMARY, MANCHESTER. REPORT OF THE WORK FROM JAN. 1, 1919, TO DEC. 31, 1919. ARTHUR BARROWS, *Radium* **16:1** (Oct.) 1920.

During the year, 677 patients have presented themselves at the institute. Of the number, fifty-one patients with malignant disease (exclusive of rodent ulcer) were rendered free from symptoms and signs. This represents 11.5 per cent. of the total cancerous cases seen, or 14.8 per cent. of cases under the heading "Too early or abandoned treatment" are excluded. The 51 cases consisted of 1 case of carcinoma of the body of the uterus, 8 of carcinoma of the breast, 19 of carcinoma of the cervix uteri, 2 of carcinoma of glands, 1 of carcinoma of the lip, 5 of carcinoma of the mouth and tongue, 7 of carcinoma of the skin, 2 of carcinoma of the vulva, 3 of sarcoma, and 3 of endothelioma.

Hitherto, the results obtained in carcinoma of the mouth have been unsatisfactory from the point of view of radium treatment. The general considerations which adversely influence radium treatment, namely, (1) large size of the growth with extensive infiltrations, (2) deficient blood supply of the tumor, (3) involvement of or adherence to bone, (4) rapid dissemination, and (5) sepsis, are commonly exhibited by malignant growths of the mouth. In carcinoma of this region, the method (Memorial Hospital, New York) of burying small emanation tubes without attempt to recover them, appears to be the best procedure yet devised. Stevenson's and Jolly's needles (0.3 mm. of steel thick) seem to be next in value.

The conditions which respond best to radium treatment are rodent ulcer, carcinoma of the skin, carcinoma of the breast, carcinoma of the cervix uteri, carcinoma of the body of the uterus, endothelioma of the parotid gland, and sarcoma of the nasopharynx. They have two factors in common, accessibility and the ability to withstand large doses of radium. Endothelioma and sarcoma seem to have a peculiar local susceptibility to radium.

Carcinoma of the rectum and melanotic sarcoma do not respond well, as a rule, to radium treatment.

Should metastasis reach the chest or other distant regions, the case is practically hopeless from the point of view of general prognosis. Metastases

in the glands of the neck may be treated by burying, for from six to forty-eight hours, considerable doses of radium emanation, i. e., tubes of from 10 to 25 millicuries screened by 0.3 mm. of platinum or 0.7 mm. of silver. In addition, tubes should be buried along the course of the cervical lymphatics. Apparent success from this treatment should be followed by irradiation of the neck by radium plates or roentgen rays.

MICHAEL, Houston, Texas.

A REPORT ON THE GYNOCARDATE AND MORRHUATE TREATMENT OF LEPROSY BASED ON FORTY CASES TREATED IN THE KASHMIR STATE LEPROSY HOSPITAL. ERNEST F. NEVE, Indian Med. Gaz. **55**:128 (April) 1920.

Forty patients with nodular and anesthetic leprosy were selected for treatment. Those who were debilitated were not included. Twenty were given intravenous injections of gynocardate and twenty subcutaneous or intramuscular injections of sodium morrhuate.

Of the 20 patients treated with gynocardate, 1 died, 2 had fresh manifestations while under treatment, and 8 were not improved by the treatment; in 4 there was slight improvement, in 3 there was distinct improvement, and the remaining 2 were much improved. The duration of the disease was from two and one-half years to seventeen years and the duration of the treatment from five to nine months.

Of those treated with sodium morrhuate, 2 died, 2 had fresh manifestations and 8 did not improve; while in 4 there was slight improvement, in 2 there was some improvement, and 2 were much improved. The duration of the disease was from one to eighteen years, while the duration of the treatment was from two and one-half to seven months.

Neve tabulates the result of his cases as follows:

Gynocardate Treatment—	No. Cases	Per Cent.
Much improved	2	10
Improved	7	35
Not improved	11	55
Sodium Morrhuate Treatment—		
Much improved	2	10
Improved	6	30
Not improved	12	60

Neve concludes his article thus:

"1. On an average treatment of six months, about half of the patients appear to derive benefit from gynocardate and morrhuate treatment.

"2. Those not definitely improved appear to remain stationary. Only about 10 per cent. show many manifestations of the disease while under treatment, some of which have been caused by the freeing of toxins by overaction of the drug.

"3. Laryngeal and ocular leprosy require great caution in the use of these remedies."

GUTIERREZ, Manila,

A STUDY OF MERCURY INJECTIONS BY MEANS OF THE ROENTGEN RAY. H. M. COLE, SIDNEY LITTMAN and TORALD SOLLMANN, J. A. M. A. **75**:1559 (Dec. 4) 1920.

The authors report the result of their investigations, which were made with the usual clinical doses of mercury, using a sufficient number of patients to

avoid experimental accidents and difficulties. The investigation included both insoluble and soluble injections, mercuric chlorid being generally used in doses of about $\frac{1}{8}$ grain and red mercuric iodid in doses of $\frac{1}{16}$ grain to $\frac{1}{3}$ grain; the insoluble injections of calomel and mercuric salicylate in doses of from 1 to 2 grains, and 40 per cent. of gray oil in doses of from 0.125 to 0.25 c.c. The findings indicate that gray oil injections are both inefficient and dangerous, and that their use should be abandoned. Calomel injections are also dangerous. Mercuric salicylate injections, especially into the gluteal muscles, give a satisfactory absorption and present relatively little danger. The absorption of usual doses, from 1 to 2 grains, is completed on the average in four days when injected into the buttocks, and in nine days when injected into the lumbar muscles. This treatment is therefore effective. The injections may be repeated safely at these intervals. However, the absorption is not uniform in all cases, so that even with the salicylate, the patient must be watched carefully for toxic manifestations.

A patient receiving this drug should have the teeth and gums examined frequently by a physician—at least once a week. The physician should inquire as to symptoms of diarrhea and of griping pains in the bowels, and the urine should be examined weekly. On the appearance of the least trace of albumin in the urine, the use of the insoluble mercury preparation should be stopped at once. When these precautions are taken, the mercuric salicylate injections are quite safe. The authors recommend that they be employed according to the following formula:

	Gm. or C.c.
Anhydrous lanolin	40
Distilled water	10
Sweet almond oil.....	150
Calomel or mercuric salicylate.....	29
Phenol or creosote.....	20
Camphor	40

Dose: 1 c.c. equals 0.09 gm. ($1\frac{1}{2}$ grains) of mercuric salicylate or calomel.

WAUGH, Chicago.

A METHOD FOR THE QUANTITATIVE DETERMINATION OF PROTEIN IN CEREBROSPINAL FLUID. W. DENIS and J. B. AYER, Arch. Int. Med. **26**:436 (Oct.) 1920.

The test for protein which is here described is considered valuable by the authors, especially when taken in connection with other tests:

Into a test tube of about 4 c.c. capacity, 0.6 c.c. of spinal fluid are measured. To this are added 0.4 c.c. of distilled water and 1 c.c. of a 5 per cent. solution of sulphosalicylic acid. The contents of the tube are then mixed by inversion (but not by violent shaking), and after being allowed to stand for five minutes, the suspension is read by means of a suitable colorimeter against a standard protein suspension prepared at the same time as the unknown. This standard is made by adding to the test tube 3 c.c. of a solution containing 0.3 mg. of protein per c.c. and 3 c.c. of 5 per cent. sulphosalicylic acid solution. The authors' standard protein solutions have been prepared from fresh normal human blood serum.

The colorimeter best suited to this work is the small model Duboscq with 30 mm. scale.

The readings were made by means of a 100 watt tungsten lamp provided with a screen of ground glass.

Three factors influencing the accuracy of the test or rendering it worthless must be mentioned: (1) A fluid contaminated with blood enough to be visible to the eye will in normal fluids give such high protein readings as to be definitely abnormal. (2) Fluids with bacterial contamination will give unreliable results. (3) Fluids standing for long periods uncorked or with cotton plugs, even though clear, will give increasing amounts of protein from day to day. If kept corked and sterile, accurate determinations were obtained at intervals over a number of weeks.

This method is said to give results accurate to within approximately 5 per cent., the protein level for many pathologic conditions, using a normal of 35-100 mg. per 100 c.c., ranging from 50-125 mg. for inactive syphilis of the nervous system up to 400-1,300 mg. in acute meningitis.

JAMIESON, Detroit.

ZUR KLINIK UND AETIOLOGIE DER DERMATOSIS DYSMENORRHOICA SYMMETRICA (CLINICAL STUDY AND ETIOLOGY OF DERMATITIS DYSMENORRHEICA SYMMETRICA). R. POLLAND, *Arch. f. Dermat. u. Syph.* **124**:89, 1917.

Polland reviews the work previously published by Matzenauer and himself on this heretofore undescribed syndrome. He gives the more recent historical data on several of the patients studied. He mentions that a too firm adherence to symmetry is not an essential requirement for the diagnosis of the affection. Some of his recent cases have shown typical examples of the disease without symmetry, and in others some time has elapsed before the symmetrical location has shown the affection.

Polland summarizes his recent studies as follows:

1. The complete well-defined typical character of dermatitis dysmenorrhoeica symmetrica is demonstrated by the recent observations.

2. The cause of the disease is an abnormal function of the ovaries; there is an auto (parenteral) destruction of ovarian albumin which circulates in the organism and causes the dermatitis. This is demonstrated (a) by the fact that the disease is encountered only in women in whom menstruation is either entirely lacking or is differentiated from the normal by long intervals and lack of intensity; (b) by the fact that in the blood of all patients there is found certain definite lipoidal substances which are demonstrated by the reaction of Neumann and Hermann, which substances are uniformly found in the pregnant, the castrated and those in the menopause; in short, among women with absent or much reduced ovarian function; (c) the presence of such a toxic substance, which appears as a decomposition product of the ovaries is made certain by the positive results of the Abderhalden reaction using ovarian protein; (d) finally, the systematic administration of organic ovarian products has a favorable influence on the process.

3. The skin efflorescences come to the skin by way of the blood stream. The circulating toxic substance has been demonstrated and neither clinically nor pathologic-anatomically speaks in any way against this postulate. The assumption that the peripheral nerves or especially the central nervous system partakes in this is not sustained by any evidence, and is not necessary to clarify the facts of the observed manifestations. (A presentation of the subject of dermatitis dysmenorrhoeica with the report of a case, by Wise and Parkhurst, may be found in the *ARCHIVES OF DERMATOLOGY AND SYPHILOLOGY* **2**:725 (Dec.) 1920.

GOODMAN, New York

THE TREATMENT OF TUMORS BY RADIUM AND X-RAYS. NEVILLE
S. FINZI, Brit. J. Surg. 8:68 (July) 1920.

In an extensive article dealing with this subject, Finzi considers: (1) the action of radiations on tumors, (2) the forms of tumor for which radiation should be used, (3) the type of radiation to be used, (4) when and by what method it should be applied, and (5) the after-effects of radiation treatment, and how to avoid or minimize them. He classifies those forms of tumors for which radiation should be used as follows:

(a) Growths to be treated by radiation in preference to surgery—lymphosarcoma; rodent ulcer.

(b) Growths in which surgery or radiation treatment is optional (prophylactic radiation used in either case)—endothelioma which has assumed malignant characteristics; epithelioma of the lip; epithelioma of the skin (early stages); the cauliflower noninfiltrating type of epitheliomas of the tongue or palate; epithelioma of the penis (ordinary type); and carcinoma of the body of the uterus.

(c) Growths for which surgery is preferred to radiations, but for which prophylactic radiation is used—carcinoma of the breast; carcinoma of the rectum; carcinoma of the ovary; carcinoma of the cervix; epithelioma of the tonsil, floor of the mouth, larynx, skin (later stages) and anus; spindle-celled sarcoma; alveolar sarcoma; melanotic sarcoma; hypernephroma and glioma.

(d) Growths for which radiation should not be used—epithelioma of the tongue (infiltrating type); epithelioma of the vulva.

As forms of benign tumors to be treated by radiation he lists angiomas, lymphangiomas, keloids, fibromyoma of the uterus, papilloma and exophthalmic and parenchymatous goiter. The various considerations controlling the type of radiation to be used, the time and method of its employment, the action of radiations on tumors, and the effect of radium are considered in detail.

SENEAR, Chicago.

THE RESULTS OF TRIALS OF SODIUM HYDROCARPATE AND
SODIUM MORRHUATE IN THIRTEEN INDIAN ASYLUMS.
E. MUIR, Indian Med. Gaz. 55:121 (April) 1920.

In the thirteen asylums in which these drugs were tried, 183 patients were treated with sodium hydrocarbate and 117 patients were treated with sodium morrhuate. Of those treated with sodium hydrocarbate, 111 were of the anesthetic type, 49 of the mixed type and 23 of the nodular type. Of those treated with sodium morrhuate, 68 were of the anesthetic type, 32 were of a mixed type and 17 were of the nodular type. The duration of the disease varied from six months to twenty-five years, while the period of treatment varied from two months to one year.

Febrile and other reactions were recorded in only eight of the thirteen reports. Of 108 cases treated with sodium hydrocarbate, there was a positive reaction in thirty-one cases, and of eighty-one cases treated with sodium morrhuate, eighteen reactions were recorded.

The dosage of both drugs varied from 0.5 c.c. to 5 c.c. of a 3 per cent. solution, beginning with the smaller dose and gradually increasing to the larger. Injections with the hydrocarbate were chiefly given intravenously and morrhuate hypodermically or intramuscularly, and in some cases intravenously.

The tabulated results may be summarized as follows: Of the patients treated with sodium hydnocarpate, 3 became worse, 48 were stationary, 74 were slightly improved and 58 were much improved, or about 32 per cent. With sodium morrhuate no patients became worse, the condition of 33 remained stationary, 48 showed slight improvement and 36 were much improved. Thus 71 per cent. showed improvement, of which 31 per cent. showed much improvement.

Hydnocarpate apparently was the better drug in anesthetic cases, but it soon blocked the veins and sodium morrhuate then had to be resorted to. In nodular leprosy, as good results are obtained with sodium morrhuate as with sodium hydnocarpate.

The results are encouraging when one considers the fact that the patients treated were from the asylums and hence most of them were in an advanced stage of the disease. The period of observation has not been long enough, which affects the results recorded.

GUTIERREZ, Manila,

THE LEONARD PRIZE FOR RESEARCH. Committee of A. W. CRANE, P. M. HICKEY and HENRY K. PANCOAST, *Am. J. Roentgenol.* 7:1, 1920.

The American Roentgen Ray Society will award \$1,000 to the author of the best piece of original research in the field of roentgen ray, radium or radioactivity. The competition is open to any one in the United States or its possessions, in Canada, Mexico, Central or South America, Cuba or other islands of the Western Hemisphere. The research matter must be submitted in literary form in the English language not later than July 1, 1921, and must not have been published. Each paper must be signed by motto and must be accompanied by a sealed envelope containing the motto and name, so that the identity of the author may be disclosed after the award has been made. In case a demonstration of an invention or method is necessary, it may be necessary to know the identity of the author before the award is made.

The field of research includes discovery, invention, improvement of method or investigations to prove or disprove any theory or problem, whether old or new, which has a direct bearing on the use of roentgen rays, radium or other radioactive substances.

The prize is offered in an altruistic spirit for the promotion of useful research, with the approval of the National Research Council. It commemorates the name of a martyred member of the American Roentgen Ray Society, Dr. Charles Lester Leonard, who paid the supreme penalty for his pioneer research in the field of roentgen ray.

GOODMAN, New York.

SODIUM MORRHUATE TREATMENT OF TUBERCULOSIS. P. GANGULI, *Indian Med. Gaz.* 55:130 (April) 1920.

This article, which shows a distinct advancement in the treatment of tuberculosis, is full of important notes and suggestions relative to the treatment of this disease. Thirty-seven patients were treated. The conditions may be classified as follows:

Group	No. Cases
1. Tuberculosis of the lungs—early stage.....	4
2. Tuberculosis of the lungs—advanced.....	28
3. Tuberculous diarrhea with enlarged mesenteric glands..	1
4. Scrofulous glands	1
5. Lupus vulgaris	2
6. Lupus erythematosus	1

In the first group three patients made an uneventful recovery, that is, all physical evidence of the disease disappeared and the patients were discharged as cured. The remaining patient made the same progress, with the exception of the presence of a thickened pleura.

The second group is even more interesting than the first in that these patients were in the advanced stage of the disease; two of them died within six weeks. Treatment of the remaining twenty-six patients resulted as follows: Eight patients were cured and discharged; ten are improving and about to be discharged. In three patients the condition remained stationary. Four patients steadily lost weight; one died.

The patient in Group 3 has made no distinct improvement.

The glands in the patient in Group 4 were inoperable. The pain and tenderness disappeared after three injections, but the patient ceased to attend the clinic after the fifth injection.

In the fifth group, the two patients with lupus vulgaris (verrucous) have almost been cured. The patient with lupus erythematosus did not seem to be affected by the treatment.

The dosage in all these cases has been the same as that used in leprosy, that is, beginning with 0.5 c.c. of a 3 per cent. solution, it was gradually increased by 0.25 c.c. once or twice a week until 2 c.c. were being given; the dose was then increased by 0.5 c.c. once a week until the maximum dose of 4 c.c. was reached. Sodium hydnocarpate seemed to be more effective in the cases in which sodium morrhuate was not effective.

GUTIERREZ, Manila,

RADIUM TECHNIQUE AT THE MEMORIAL HOSPITAL, NEW YORK. GIOACCHINO FAILLA, Arch. Radiol. & Electroth. **25:3** (June) 1920.

The author, who is the physicist of the institution, gives part of the details of the methods used for the preparation and measurement of radium emanation and the active deposit of radium. The salt, itself, is never used at the Memorial Hospital. For these technical minutiae, which would be practically valueless in abstract, the interested reader is referred to the original article.

The dental compound applicators devised by Janeway have proved valuable. They are made by placing dental modeling in hot water until it becomes plastic. In this state, it is applied over the lesion, molded into the desired shape, and left in place until it has cooled and hardened. Grooves are then cut into the mold with a hot tool, and into these silver tubes containing radium emanation are placed and retained by paraffin. In this way, dosage, distribution, and the protection of normal tissue are readily obtained.

A method that has proved effective is the introduction of bare emanation tubes into tumor masses. The tubes are allowed to decay in situ.

Gamma ray applicators in the form of a flat box 7 by 10 cm., with a bottom of lead 2 mm. thick, are often used for the treatment of large and deep growths. These packs, as they are called at the Memorial Hospital, have many rows of headless nails between which silver emanation tubes can be fitted.

Other ingenious apparatus of the same type to meet special indications are described.

Very good results have been obtained by the intravenous use of the active deposit of radium in lymphatic and myelogenous leukemia, Hodgkin's disease, and lymphosarcoma.

MICHAEL, Houston, Texas.

UEBER SPIROCHAETENBEFUNDE IN LYMPHDRUESSEN (CONCERNING THE DEMONSTRATION OF SPIROCHETES IN THE LYMPH NODES). RICHARD FRUEHWALD, *Wien. klin. Wchnschr.* **33**: 999, 1920.

The lymph nodes play an important rôle in the pathology of syphilis. Their reaction clinically is sufficiently characteristic in many instances to vouchsafe a diagnosis on it alone. The persistence of their enlargement is an important item in latent syphilis.

Fruehwald has performed node puncture 89 times among 83 syphilitics, of whom 24 were in the primary stage, 18 in the beginning of the secondary, 27 in later secondary, 4 in tertiary, and 10 in the latent phases. Among the twenty-four primary cases, spirochetes were demonstrated by node puncture in twenty cases. The negative cases were not characterized by any notable differences from those that gave positive results. Of the eighteen patients, who, in addition to the evidence of primary syphilis, also showed exanthema, only seven showed spirochetes on node puncture. This finding agrees with the evidence of others that in the active secondary stage the lymph nodes are less likely to harbor the organism. In the later cases, there were but seven positive findings as against twenty negative node punctures. The duration of the disease among the seven positive cases was from four to six months for five patients, one year for one patient, and two years for another patient. Among the four tertiary cases, the spirochetes were not demonstrated. Among fourteen treated cases of syphilis, the spirochetes were demonstrated by node puncture three times. One of the patients had received nineteen mercurial rubs, a second of the three had had 0.7 gm. of old arsphenamin intramuscularly. The third patient had had three "mercurial cures" during the three years of his disease. The regional nodes were selected in all these cases.

In five instances the epitrochlear node was punctured with positive results in two, the first with chancre and exanthem, the second with recurrent secondaries in an untreated woman. The submaxillary was also punctured with negative findings in two cases of gumma of the tonsil, and in one case of chancre of the chin.

A review of the findings shows that in the primary stage and the early eruptive period, the nodes lodge the spirochetes in a large percentage of the cases. In the later secondary stage, and also in the period of recurrent lesions, even if some time has elapsed since the acquisition of the disease, the regional nodes give positive results on puncture for spirochetes. It was also feasible to show the infectiousness of the nodes other than the regional in a number of cases. The finding of the spirochetes in latent syphilis is of especial significance when one considers that three years had elapsed since the disease was first acquired (in one case of Fruehwald's and in several reported in the literature). There may be some connection not yet fully understood between the persistence of spirochetes in the nodes and recurrent lesions of syphilis. The nodes may act as a source of supply to the blood stream.

GOODMAN, New York.

A CLINICAL STUDY OF WASSERMANN-FAST SYPHILIS, WITH SPECIAL REFERENCE TO PROGNOSIS AND TREATMENT. J. H. STOKES and G. J. BUSMAN, *Am. J. M. Sc.* **160**:658 (Nov.) 1920.

The authors discuss a much debated point in the observation of syphilitics and draw some interesting conclusions. Of 458 syphilitics studied and treated

for varying periods, they found 66 per cent. of primary and secondary cases, and 22 per cent. of latent, late and hereditary cases had an unchanged positive Wassermann reaction. These persistent positive reactions were, in 44 per cent., due to cardiovascular changes, while next in order of frequency were neurosyphilis, osseous lesions, hepatic, splenic, gastric and miscellaneous types. It was also found that individual cases of this group showed more than one type of involvement while cardiovascular syphilis showed 65 per cent. aortitis, 60 per cent. myocardial change, neurosyphilis showed 40 per cent. paresis, 50 per cent. tabes, half of these patients also having cardiovascular involvement. Cutaneous syphilis was not associated with neurosyphilis, and while foci of pyogenic infection were found in many cases, the authors did not believe any definite connection could be traced as a cause of the persistent positive reaction.

They do not state any definite amount of treatment these patients should receive although the great majority of treated cases are symptomatically cured or arrested. While a negative Wassermann reaction is desirable, it is unwise to subject the patient to too long or continuous treatment in order to change the reaction. Symptomatic cure with administration of as much treatment as to an early case, if possible, will generally be sufficient, provided periodic examination be conducted through life, especially with regard to the cardiovascular and nervous systems.

JAMIESON, Detroit.

RECHERCHES SUR LE LIQUIDE CEPHALO-RACHIDIEN DANS LA PERIODE PRIMAIRE DE LA SYPHILIS (STUDIES OF THE CEREBROSPINAL FLUID IN PRIMARY SYPHILIS). S. NICOLAU, *Ann. de dermat. et syph.* 7:200 (July) 1919.

In this interesting article, the author's observations cover fifty-one cases of absolutely primary syphilis. None of the patients presented any secondary or nervous manifestations. In the 51 cases, 18 patients had lymphocytosis; in 9 it was discrete, the number of cells varying from 7 to 18; in 5 moderate, the cells varying from 22 to 39; and in 4 it was notable, the cells varying from 40 to 60. Lymphocytosis made its appearance in the beginning of the third week; it therefore constitutes, next to adenopathy, the earliest manifestation of general infection. It also demonstrates the special affinity which exists between the spirochete and the central nervous system. Of the eighteen patients with cerebrospinal lymphocytosis, inequality of the pupils was noted in eleven. Of the thirty-three primary cases in which the patients did not have lymphocytosis, the pupillary inequality was limited to five. Nicolau therefore concludes that inequality of the pupils may be considered as a presumptive sign of cerebrospinal lymphocytosis. The lymphocytosis progressively increased with the approach of the secondary period. In only one case did treatment cause it to disappear. In three cases its development was arrested. In the balance of the cases the development of the lymphocytosis seemed to be in no way affected by the treatment, even though it was sufficiently intensive in character to suppress all secondary manifestations. The author believes that abortive treatment, in order to be effective, must be administered before the third week. Suppression of the secondary period, with a persistent negative Wassermann reaction, is not alone to be depended on. There must also be evidence of nonirritation in the cerebrospinal fluid.

BECHET, New York.

ELEPHANTIASIS CONGENITA ANGIOMATOSA (UNNA) ASSOCIATED WITH CHANGES IN THE CAPILLARIES. MILO K. MILLES and KARL M. NELSON, *Am. J. Dis. Child.* **20**:127 (Aug.) 1920.

A boy, aged 6, was admitted to the hospital with a marked dilatation of the veins of the right thigh, leg, scrotum and penis. The mother noticed the swelling when the patient was 2 weeks old. At the time of examination, the venous enlargement behind formed tumorlike masses, beginning to the right of the scrotum, covering the entire buttocks and extending over practically the entire outer aspect of the thigh and leg, being particularly marked from the knee down. Greatly dilated veins stood out on the dorsum, the outer aspect of the foot, and extended about half way across the plantar surface.

The swelling felt soft, elastic, and velvety; over the foot it was more lobulated and wormy. The summits of the irregularity were bluish. They were turgescient, but not erectile. The blood could be pressed out leaving an apparently normal, delicate skin. The tumor did not pulsate. The limitation from the surrounding skin was fairly well defined. In several planes, thrombi could be felt. The vascular masses became intensely engorged on standing. There was a mass of dilated deep veins on the scrotum, penis, and a small mass of hemorrhoidal veins. One small angioma about the size of a pinhead was situated on the right nostril. The blood Wassermann reaction was negative, and the eyegrounds were negative.

Histologically, the lesions are found in the superficial layers of the corium. They may extend deeply and involve the subcutaneous tissue. The venous capillaries are chiefly involved. Thickening of the walls of the veins is followed by endothelial proliferation. Elastic fibers and muscular fibers are absent.

By utilizing the method of Weiss to study the capillaries in the manifolds of the fingers, three striking differences from normal children and adults were noted: (1) The loops were irregularly arranged. (2) The number of loops was distinctly greater than in other cases. (3) The loops were less sharply defined, and not well developed. They appeared to be stunted.

The capillaries were abnormal for the age of the patient. The presence of abnormality of a part of the vascular system in the case described suggests a relationship between this abnormality and the lesion. One can think of a direct causal relationship so that the abnormality of the vessels in conjunction with some local factor enters directly into the production of the lesion.

Photographs of the case, and illustrations of the capillary changes accompany this presentation of a rare disease, of which Unna mentions two cases.

(It has appeared particularly well worth while in this relation to reread the notes by Unna on the disease, and especially his introductory remarks on the etiology of the affection. Unna: *The Histopathology of the Diseases of the Skin*, Translated by Norman Walker, 1896, p. 1168.)

GOODMAN, New York.

THE TREATMENT OF LEPROSY WITH THE DEAN DERIVATIVES OF CHAULMOOGRA OIL. J. F. McDONALD, *J. A. M. A.* **75**:1483 (Nov. 27) 1920.

McDonald gives an interesting report of the treatment of leprosy with the Dean derivatives of chaulmoogra oil, with an apparent cure in seventy-eight cases. Standard treatment for weekly intramuscular injection consists in the

use of the ethyl esters of the entire fatty acids of the whole oil with 2 per cent. of iodine by weight chemically combined, the dosage of which begins with 1 c.c. and is increased by 1 c.c. at every second or third injection until a dosage of from 2 to 6 c.c. is reached, according to the age and weight of the patient. Internally, patients receive in capsule form the mixed fatty acid carrying 2.5 per cent. of iodine in chemical combination; they receive the fatty acids rather than their ethyl esters because they better conform to the normal digestive process which precedes fat absorption. McDonald is therefore using by mouth a predigestive oil or fat which is semisolid, at room temperature, and in capsule form easy to take. Its dosage begins with $\frac{1}{6}$ gm. per hundred pounds of the patient's weight, three times a day, an hour or two after meals. This dosage is increased every two weeks until a maximum of 1 gm. per hundred pounds of weight per dose is reached. Of these two forms of administration, McDonald regards treatment by injection as the more important. In 6,924 deep injections, there was only one case of resulting abscess.

WAUGH, Chicago.

A CONTINUATION FROM 1918 OF THE REPORT ON PATIENTS WITH LEPROSY IN BANKOK, TREATED WITH SODIUM GYNO-CARDATE "A." M. CATHEW, Indian Med. Gaz. 55:134 (April) 1920.

This article may be briefly summarized in the following table:

Case	April, 1917 Duration	Bact.	Type	April, 1918 Results	September, 1919 Results
1	6 years	Maculo-anesthetic	Much improved	Almost complete disappearance
2	Has disappeared				
3	1 year	Positive	Maculo-anesthetic	July, 1918, improved	Trophic ulcer, otherwise improvement over 1918
4	8 years	Positive	Mixed	Complete disappearance of lesions	No relapses
5	Has disappeared				
6	2 years	++	Maculo-anesthetic	Complete disappearance of lesions	Retrogression over 1918. Bact. ++
7	2 years	+	Maculo-anesthetic	Considerable improvement	Complete disappearance of lesions
8	15 years Oct., 1917	Mixed	Marked improvement	Complete disappearance of lesions
9	2 years Oct., 1917	Maculo-anesthetic	Considerable improvement	Marked improvement
10	Has disappeared				
11	Has disappeared				
12	1 year Nov., 1917	Mixed	Considerable improvement	Great improvement
13	2 years Feb., 1918	Maculo-anesthetic	June. Marked improvement	Great improvement
14	6 years May, 1918	Maculo-anesthetic	Reaction	Marked improvement
15	For a long time		Mixed	All clinical symptoms have disappeared
16	7 years Aug., 1918	Maculo-anesthetic	May, 1919. Slight improvement
17	21 years May, 1919	Maculo-anesthetic	Marked improvement
18	9 years	Tubercular	June. Marked improvement

GUTIERREZ, Manila,

REINFEKTIONEN UND RESIDUALSKLEROSEN. EIN BEITRAG ZUR FRAGE DER HEILBARKEIT LUETISCHER INFEKTIONEN DURCH SALVARSAN (REINFECTION AND RESIDUAL SCLEROSIS. A CONTRIBUTION TO THE QUESTION OF THE CURABILITY OF SYPHILIS WITH ARSPHENAMIN). RUDOLF MUELLER, Arch. f. Dermat. u. Syph. **123**:593, 1916.

Chancriform recurrent lesions may simulate the initial lesion of a supposed reinfection. According to Bernario the following items must be met before a diagnosis of reinfection can be accepted. Of the supposed reinfection: (1) positive clinical diagnosis of the primary lesion, (2) demonstration of the *Spirochaeta pallida*, (3) regional node enlargement, (4) subsequent positive Wassermann reaction, and (5) recognition of the source of the infection.

The cases which Mueller studied, and on which he bases his personal opinion that most of the cited instances of reinfection are in reality cases of monorecicide were twenty-six in number, and occurred in his regimental unit from September, 1914, to March, 1916. Few of the patients received treatment which would be accepted as adequate today—three doses of neo-arsphenamin and fifteen rubs constituted average treatment, although many of the patients had but one injection of the arsenic preparation, and a few others as many as five. Observations of this character are of historical interest, but do not add materially to the modern problem of the curability of syphilis, and the possibility of reinfection. That Mueller recognized these facts may be judged by his appeal that all cases of reinfection or supposed reinfection be reported in order that definite conclusions in regard to the problem be feasible in the future.

GOODMAN, New York.

PER LA CONOSCENZA DEL L'EPITELIOMA ADENOIDE CISTICO (BROCKE) TRICHOEPITHELIOMA PAPILLOSUM MULTIPLEX (JARISH). L. TONACA, Riforma med. **36**:43 (Oct.) 1920.

Tonaca reports the case of a man, 27 years old, who presented small, hard and firm nodules on the forehead, the back, the nose, the axillae and the scalp. These nodules were of normal color, and the patient complained of no subjective symptoms. Histologic examination showed that the tumor was formed by the aggregation of numerous epithelial lobules surrounded by abundant connective tissue. The epithelial cells were oval, with elongated nuclei and little protoplasm. These cells were arranged in rows at the periphery of the nodules, enclosing a mass of epithelial cells of similar type but without special arrangement. Kariokinetic figures were abundant. Rows of long epithelial cells could be seen here and there in the nodules. In the center of the epithelial mass a small cavity was always present, sometimes empty, sometimes filled with an amorphous substance. Numerous granules of pigment could be seen in the epithelial cells, as well as in the cavities. The skin covering the nodules appeared practically normal; only a few nests of epithelial cells similar to those of the tumors could be detected near the hair follicles. The author feels inclined to believe that these tumors originate in the epithelial elements of the pilosebaceous follicles.

PARDO-CASTELLO, Havana.

LYMPHOGRANULOMATOSIS CUTIS. JAMES STRANDBERG, *Acta Dermat.-Vener.* **1:215** (Oct.) 1920.

In a lengthy paper, with a large and excellent bibliography, Strandberg reviews the literature on the subject of lymphogranulomatosis cutis and adds a recent case of his own to the list. In the cases formerly reported, he found the following types of cutaneous changes:

1. Small, brownish-red, flattened papules of a rather firm consistence, scattered or confluent and sometimes breaking down.

2. Larger tumors, more deeply seated and of a bluish-brown to bluish-green color, which may ulcerate.

3. Deeper, more diffuse infiltrations, frequently found only by palpation.

His patient presented the small brownish papular type of eruption, which was localized on the trunk and arms, the lesions occurring singly and in patches. There was no pruritus. Cervical lymph nodes were palpable. The peculiarities of the case are:

1. The advanced age of the patient, 68 years, as compared with the average, 20 to 35 years.

2. The strongly positive tuberculin reaction.

3. The histologic examination of the glandular and cutaneous tumors showing a granulation tissue containing giant cells of both Sternberg's and Langhans' type.

The possibility of a tuberculous etiology is discussed, and it is suggested that the Sternberg giant cell may be developed from the giant cell of Langhans. Strandberg does not think that his case throws any light on the question of the etiology of the condition.

PARKHURST, New York.

THE AFTER-TREATMENT OF LEPROSY. E. MUIR, *Indian Med. Gaz.* **55:134** (April) 1920.

In view of the patients who for months have shown no signs or symptoms of the disease, who have either had a relapse or who have shown marked reaction to sodium morrhuate, Muir defines the after-treatment as commencing when all the symptoms have disappeared and the patient is able to return to work. The analogy is shown between leprosy and tuberculosis, in which the bacilli, after remaining dormant unsuspected for a long time may renew their activity when the resistance of the patient is lowered. Treatment must therefore be continued for a long time and the patients must be kept under observation for many years. After treatment with injections, the patients may carry on their own treatment at home by taking pills of sodium morrhuate or sodium hydnocarpate. Muir believes that there is cumulative action of the drug, and this must be borne in mind, so that before patients are discharged from the hospitals they have a sufficient amount of the drug in their systems to produce a favorable action on the disease.

GUTIERREZ, Manila,

LA KERATOSE BLENNORRHAGIQUE (GONORRHEAL KERATOSIS). TRÉMOLIÈRES, *Ann. de dermat. et syph.* **7:145** (May) 1919.

The author believes that keratosis almost invariably occurs in grave cases of gonorrhea, with associated arthropathy, cardiorenal disease and other evidences of gonorrheal septicemia. It appears in three forms: isolated cornified

papules, aggregated papules and complete keratosis. It first appears on the dorsal surface of the foot and great toe as small, rounded papules, in the center of which is a conical, horny elevation. In the later stages of the disease the skin becomes so keratotic that it resembles somewhat a geographical map in relief. The nails are often thickened, striated and deformed. They frequently become detached. In spite of the fact that the gonococcus has not been demonstrated in the lesions, the author favors the theory of local infection rather than that of nervous origin. Macerations of the skin as a result of local applications and immobilization of the feet and legs as a result of arthropathies, with predisposition to keratosis, are contributing factors. One of the patients mentioned had had an immense overgrowth of plantar epidermis previous to the appearance of gonorrheal infection. The author believes that the vaccine of Nicolle and Blaizot is a specific in the treatment of the disease, both for the keratosis and the gonorrheal infection itself.

BECHET, New York.

DER BLUT BEFUND BEI DER EPIDERMOLYSIS BULLOSA HEREDITARIA (BLOOD FINDINGS IN EPIDERMOLYSIS BULLOSA HEREDITARIA). BODO SPIETHOFF, Arch. f. Dermat. u. Syph. **123**:877. 1916.

Isolated blood examinations made casually on cases of epidermolysis do not indicate the true state of affairs. Only repeated examinations on the same patient, and on members of the family (even those that do not show the symptoms of the disease) lead to definite findings. Spiethoff has made such a study.

All cases of epidermolysis bullosa hereditaria in a family showed the same blood picture. These changes are not the same at every period. Variations appear in every case. The essentials of the blood changes are: disturbance in the neutrophil picture—lowered differential; essential increase in the large mononuclear and transitional cells—also the occurrence of periods of normal counts; increase in differential, or differential and total lymphocyte count, with occasional periods of decrease in these cells; occasional giant cells with pathologic forms of lymphocytes; similar blood picture disturbance is noticed in other members of the family even if they have evidenced no symptom of the disease. This leads to the conclusion that the disease is due to an inherited cause which does not always manifest itself on the skin. The similarity between the blood picture of epidermolysis and certain endocrine disturbances may mean a causal relation.

GOODMAN, New York.

THE HIGHER FUNGI IN RELATION TO HUMAN PATHOLOGY (THE MILROY LECTURES). A. CASTELLANI, J. Trop. M. **23**:10 (May 1) 1920; *ibid.* **23**:117 (May 15) 1920; *ibid.* **23**:133 (June 1) 1920.

The first two lectures deal with the morphology, classification, biologic and biochemical properties of the higher fungi, discussing the so-called internal mycoses—thrush, bronchomycoses, tonsillomycoses, certain mycoses of the nervous system and of the urogenital system.

The third lecture deals with the trichomycoses and dermatomycoses. The first group includes aspergillomycoses of the beard and trichomycoses axillaris, flava, rubra et nigra, the yellow variety being due to a fungus of the genus *nocardia*, the black and red types being due to the added infection producing black or red pigment.

Tinea flava and *tinea nigra* are tropical mycoses producing yellowish and black patches, respectively. *Cryptococcosis epidermica* consists of brownish, dirty looking patches which could not be removed with soap and water.

Accladiosis produces ulcerative lesions all over the body, generally rounded and sharply marked. The ulcers are later covered with a bright yellow crust from dried secretion. Potassium iodid is generally sufficient for a cure.

Blastomycoses, Dhobie itch and *tinea imbricata* are also discussed.

JAMIESON, Detroit.

BLASTOMYCOSIS: WITH REPORT OF A CASE DYING FROM
ABSCESS OF THE BRAIN. JOHN T. MOORE, Surg., Gynec. & Obst.
31:590, 1920.

The case reported by Moore occurred in a youth of 17, who was in the habit of carrying splinters in his mouth. The diagnosis was not made at first by the dentist consulted, who referred him to a physician. Wassermann reactions were made, and roentgenograms taken with negative findings. Examinations of the pus disclosed the blastomycetes. Despite operative interference, which is admitted was not radical, and the use of roentgen-ray therapy, the patient showed new lesions with sinus formation about the orbit. Local treatment and enucleation did not prevent metastasis. Signs of cerebral involvement intervened and the patient died. Sections of the brain showed abscess cavities. The infection of the brain was possibly through the ophthalmic vein or through the veins of the scalp and the emissary veins through the skull. The study of the organisms in the different lesions and tissues showed a considerable variation in their size; those from the abscess of the face, neck and orbit showing the large forms, while no large forms could be found either in the pus or the tissue from the brain.

GOODMAN, New York.

THE TREATMENT OF ALOPECIA AREATA WITH QUARTZ LAMPS
(KROMAYER AND ALPINE). HOWARD FOX, Med. Rec. **98:895**.
(Nov.) 1920.

In his series of fifty cases, the author used the Kromayer lamp for localized areas and the Alpine lamp for generalized. Cleansing the skin with alcohol prior to the treatment shortens the time required for the production of erythema. The patients were treated at intervals of one week and in such dosage as would produce an erythema lasting a week. Ages ranged from 4 to 50 years, all were scalp cases, and the disease had existed from one week to eight years. The degree of hair loss varied from a single area to complete alopecia. Twenty-seven cases are reported as cured, twelve improved and eleven unimproved. Commenting on his results the author says they were better than would appear from the tabulation in that most of the cases classified as unimproved had not been treated sufficiently. The results are considered more satisfactory than by other methods.

TOMLINSON, Omaha.

THE RELATION OF FOOD TO INFANTILE ECZEMA. E. S. O'KEEFE,
Boston M. & S. J. **183:569** (Nov. 11) 1920.

The author reports seventy cases of eczema in children under 4 years of age, treated by the Children's Medical Out-Patient Department of the Massachusetts General Hospital, in conjunction with the Dermatological Department.

Skin tests were performed on the backs of these children. His tables show that 41 per cent. gave a positive reaction to one or more food tests. Egg proteins gave a positive reaction in 30 per cent. of the cases in which they were tried. Twenty per cent. of the series gave a history of asthma, eczema or urticaria in some other member of the family. The mother in no instance showed sensitization to the protein to which her child reacted. His work in regard to sensitization in exclusively breast fed infants is extremely interesting. He believes that these intimate relations between foods and eczemas in so large a percentage justifies the conclusion that the dietary regulation is essential in the treatment of this condition, and that the protein skin tests give information which can be obtained in no other way, though they do not supplant the older methods of determining what does and what does not agree with a particular infant.

LANE, Boston.

EIN FALL VON AUSGEBREITETEM BROMEXANTHEM BEI EINEM PSORATIKER (A CASE OF GENERALIZED BROMODERMA IN A PSORIATIC PATIENT). JAMES STRANDBERG, Arch. f. Dermat. u. Syph. **123**:1067, 1916.

An officer of the navy, who had been a sufferer from psoriasis, showed symptoms of ulcer of the stomach. He was given bromids in a dosage of from 1 to 3 gm. a day to relieve nervous symptoms. About four months later, he had an eruption which began on the face and extremities and soon extended to the trunk. The lesions were of varying size, deep red or violet, and very itchy. After fourteen days, the eruption had become general. There were papular lesions about the size of a pea and plaques almost the size of a palm. No scales, folliculitis or pustules were found. The similarity to bromoderma was demonstrated, and despite the period between ingestion and cutaneous manifestation, the condition was believed to be bromoderma. Strandberg mentions that it had previously been reported that persons with disease of the intestinal tract were more susceptible to bromoderma than others, and he cautions us to be more careful in the administration of the drug.

GOODMAN, New York.

ACTINOMYCOSIS TREATED WITH METHYLENE BLUE AND ROENTGEN RAY. VIGGO W. JENSEN and C. W. SCHERY, J. A. M. A. **75**:1470 (Nov. 27) 1920.

In the case cited by the authors methylene blue was given internally, as well as injected locally in a 3 per cent. solution into the cheek. The internal administration was begun with 2 grain doses, three times a day, and later increased to 5 grains, four times a day. This therapy caused nausea, dizziness and weakness at first, but these symptoms soon disappeared. On the twelfth day of treatment the process flared up, involving the orbit and causing complete closure of the eye. It was thought advisable to make use of the roentgen ray, and an erythema dose was used consisting of an exposure of two minutes to a 6 milliampere, 6 inch spark gap with the target 10 inches distant without a filter except over the upper part. This treatment was followed by a cessation of the acute symptoms, and the local edema decreased. A few sinuses remained in the large area, and two large abscesses formed just below the eye. These were incised and kept wide open. A second

roentgen-ray treatment was applied, with similar local and constitutional results, but the process receded so rapidly that on the forty-third day all treatment was stopped as all the sinuses, edema and induration had disappeared.

WAUGH, Chicago.

DIE LUESREAKTIONEN VON MEINICKE UND SACHS-GEORGI IN DER INNEREN MEDIZIN (THE SYPHILIS TESTS OF MEINICKE AND SACHS-GEORGI IN INTERNAL MEDICINE). KARL HAJOS and BELA MOLNAR, JR., Wien. klin. Wchnschr. **33**:966, 1920.

The Meinicke and the Wassermann reactions were paralleled in 537 cases; the Sachs-Georgi and the Wassermann reactions in 538 cases. The following conclusions are given: The Meinicke, and especially the Sachs-Georgi, reactions are performed with much simpler methods than the Wassermann reaction, and there are not the difficulties of procuring the proper materials. The delicacy of both reactions appears to be slightly less than that of the Wassermann reaction. The Meinicke reaction is slightly less specific than the Wassermann, but the Sachs-Georgi approximates it. The Sachs-Georgi is feasible with cerebrospinal fluid, but the fluid cannot be investigated with the Meinicke reaction. For the time being, neither can replace the Wassermann reaction, but the Sachs-Georgi supplements it, and both may be utilized together to advantage.

GOODMAN, New York.

ON THE REACTION OF PREGNANT AND LACTATING FEMALES TO INOCULATION WITH SPIROCHAETA PALLIDA—A PRELIMINARY NOTE. WADE H. BROWN and LOUISE PEARCE, Am. J. Syph. **4**:593 (Oct.) 1920.

This article is the report of an effort to determine whether or not there is a difference in the reaction of a pregnant female and a normal animal to local inoculation with *Spirochaeta pallida*.

The authors conducted a series of experiments on rabbits. Their results show that there is a decided difference in the reactions and that this difference exists through the period of pregnancy and during the greater part of the period of lactation.

In most instances the pregnant animal offered a defensive mechanism which inhibited clinical evidence of infection. In a few others, slight local reactions and marked constitutional disturbance seemed to show an ineffectual resistance to the infection.

TOMLINSON, Omaha.

A POSITIVE WASSERMANN TEST IN NONSYPHILITIC PATIENTS AFTER INTRAVENOUS THERAPY. ALBERT STRICKLER, HENRY G. MUNSON and DAVID M. SIDLICK, J. A. M. A. **75**:1488 (Nov. 27) 1920.

The authors assert that a positive complement-fixation test for syphilis, obtained with the serum of a patient treated with arsphenamin for some non-syphilitic malady or some obscure disease, should be interpreted with great caution and considerable reservation. In view of the fact that there are a number of conditions, such as anemia, malaria, recurrent fever, pemphigus, psoriasis and septicemia, in which arsphenamin is recommended as a method

of treatment, and because arsphenamin is employed as a last resort, at times in the treatment of obscure diseases and conditions difficult to influence, it becomes the duty of the clinician and the serologist not to be too hasty or too dogmatic in pronouncing such a person definitely syphilitic. The authors believe that at times too much arsphenamin is administered in the treatment of syphilis, and that this remedy may be responsible for the persistence of a positive Wassermann reaction.

WAUGH, Chicago.

PERMEABILITE ET REACTION MENINGEES: INDEX DE PERMEABILITE (MENINGEAL PERMEABILITY AND REACTION: THE INDEX OF PERMEABILITY). O. MICHAELIS, *Acta Dermat.-Vener.* **1**:186 (Oct.) 1920.

The degree of permeability of the meninges to syphilitic antibodies from the blood stream is apparently dependent on the degree of inflammation which the meninges may have suffered. In a syphilitic patient a hitherto negative spinal fluid may become positive after an attack of typhoid fever, for example, or after an intraspinal injection of arsphenamized serum.

In the quantitative Wassermann reaction, the minimum for a positive result in the blood serum and in the spinal fluid usually differs, and in a ratio which the author has called the "index of permeability," to a certain extent characteristic for each form of syphilis of the central nervous system. This may often solve difficult questions of differential diagnosis, if we also take careful note of the pressure of the fluid, the cell count, the quantity of albumin and the presence of globulin.

PARKHURST, New York.

EIN FALL VON DERMATITIS ERYTHEMATO-PAPULOSA ATROPHICANS MACULATA CHRONICA (A CASE OF DERMATITIS ERYTHEMATOPAPULOSA ATROPHICANS MACULATA CHRONICA). S. MENDES DA COSTA and PAPEGAAY, *Acta Dermat.-Vener.* **1**:175 (Oct.) 1920.

A farmer, 57 years of age, had suffered for twenty-seven years with a generalized erythroderma leading to macular cutaneous atrophy. As a part of the picture, on the extremities and buttocks papules appeared from the size of a pea to that of a bean, of slow development and usually terminating in necrosis. An additional feature was the formation of keratomas and epitheliomas.

Histologic examination revealed a polymorphous cellular infiltration in the derma, with some giant cells in the papular lesions. There was a tendency to disappearance of the elastic tissue.

In the differential diagnosis the authors rule out premycotic erythroderma, lymphoderma cutis, xeroderma pigmentosum, pellagra, infectious angioma and a number of rare conditions.

PARKHURST, New York.

XANTHOMA DIABETICORUM. W. KNOWSLEY SIBLEY, *Proc. Roy. Soc.* **2**:3 (Sept.) 1920.

A case report.

Guy, Pittsburgh.

CONTRIBUTION A L'ETUDE DES TUBERCULOSES CUTANÉES HEMATOGENES DIFFUSES, A TYPE ERUPTIF, CLINIQUEMENT ATYPIQUES (DIFFUSED HEMATOGENOUS CUTANEOUS TUBERCULOSIS, OF ERUPTIVE TYPE, AND CLINICALLY ATYPICAL). JADER CAPPELLI, *Ann. de dermat. et syph.* **7:257** (Sept.) 1919.

The author reports in great detail a case illustrative of the disease. The lesions were symmetrical and of general distribution. They consisted mostly of nodules, from the size of a millet seed to that of a lentil, of a yellowish-red color on the upper trunk, and violaceous on the legs. They were polygonal in shape, with depressed centers, not unlike lichen planus. Other lesions were conical, surmounted by a vesicopustule; others were macular, and of a brownish red color. A suppurating cervical adenitis was present. The cutireaction with old tuberculin (Koch) was positive. Guinea-pig inoculation with pus from the cervical glands, and an emulsion made from the skin lesions, gave positive results.

BECHET, New York.

SOBRE LA HEREDOSIFILIS Y LA REACCION DE WASSERMANN (THE WASSERMANN TEST IN HEREDITARY SYPHILIS). M. J. BARILARI and W. KARMIN, *Prensa med., Argentina* **7:7** (Aug.) 1920.

The authors divide the lesions of hereditary syphilis into those produced by the spirochete and those produced by its toxins. In the first type of cases, the Wassermann test is always positive, in the second, the test is as a rule negative, there being no spirochetes in the body to produce specific antibodies. In the latter group of cases there are permanent physical changes due to the action of the syphilitic toxin or toxins on the tissues and organs (epilepsy, endocrine defects, malformations of the brain, etc.). The authors believe that with the technic used by most men, the Wassermann test is not accurate as a variable amount of complement is used, the quantity of alcohol in the antigen is not taken into consideration, several tests are made together and the results are read at the same time.

PARDO-CASTELLO, Havana.

UEBER POLYNEURITIS SYPHILITICA (CONCERNING POLYNEURITIS SYPHILITICA). WILHELM KERL, *Wien. klin. Wchnschr.* **33: 921**, 1920.

The number of undoubted cases of syphilitic polyneuritis is not very great. Many of the reported cases are complicated in that the patient had been under mercurial treatment before the polyneuritis developed. Kerl had one of the few cases reported of a polyneuritis which appeared several days before the eruption of generalized syphilis. The peripheral neuritis embraced the right upper and lower extremity and the right side of the face. The cerebrospinal fluid is thus reported: cells, 26; Pandy test, + + +; Nonne-Apelt reaction, + +; Nissl cells, 0.35 per cent.; colloidal gold reaction, 1/10-1/40, violet; Wassermann test, negative. The blood Wassermann test was positive. According to Steinerts, the condition described is best named "mononeuritis multiplex syphilitica."

GOODMAN, New York.

CASE OF LUPUS ERYTHEMATOSUS TREATED WITH AUTOGENOUS STREPTOCOCCAL VACCINE PREPARED FROM ENUCLEATED TONSILS. H. W. BARBER, Proc. Roy. Soc. **2:3** (Sept.) 1920.

A typical case of facial lupus erythematosus of nine years' duration had been treated by different measures with varying success. Whenever cleared, the lesions would recur. In 1919, the tonsils were removed and a pure culture of *Streptococcus longus* found in them. A vaccine was prepared and injections given at weekly intervals over a period of a little less than six months. Dosage began at 5,000,000 organisms, being gradually increased to 10,000,000. No local treatment was given. Focal reaction occurred after each treatment, and there was definite clinical improvement in the lesion.

GUY, Pittsburgh.

INTERPRETATION OF THE WASSERMANN REACTION. W. P. BOARDMAN, Boston M. & S. J. **183:537** (Nov. 4) 1920.

This is a discussion of the Wassermann reaction, emphasizing the possibility of variations in all reagents employed, and conditions causing false positive and negative reactions. Variations in the Wassermann reaction in the various stages are discussed, as well as its use as a guide in treatment. The author advocates a one, two, three plus system of reading and reporting reactions, and asserts that there is no more of a variation in the reaction than is found in the results of auscultation and percussion by various men.

LANE, Boston.

SINGOLARE OSSERVAZIONE DI CARBONCHIO CUTANEO (INTERESTING CASE OF CUTANEOUS ANTHRAX). L. MARTINOTTI, Riforma med. **36:43** (Oct.) 1920.

A farmer, 53 years old, about twenty days before his admission to the hospital had fleeced and buried a dead sheep. The lesions were on the back of both wrists in the form of ulcers of red elevated borders and of central depressed black eschar. He recovered uneventfully after a microscopic diagnosis was established. The author calls attention to the good results obtained in these cases by the use of arsphenamin and the specific serum.

PARDO-CASTELLO, Havana.

CASE OF TRICHOTILLOMANIA. E. G. LITTLE, Proc. Roy. Soc. Med. **13:9** (July) 1920.

A little girl aged $4\frac{1}{2}$ years acquired this habit at the age of 2 years. At the time of examination the right parietal area was completely bald. Dr. Whitefield suggested that the hair be clipped and kept clipped until the habit is forgotten; he had obtained a cure in this way in a similar case.

GUY, Pittsburgh.

CASE OF XANTHOMA. J. L. BUNCH, Proc. Roy. Soc. **2:3** (Sept.) 1920.
A case report.

GUY, Pittsburgh.

DERMATOLOGIC ABSTRACTS

JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION

SYPHILITIC MENINGITIS. O. CLARK, *Brazil-Medico* **34**:652 (Oct. 2) 1920.

Clark's patient presented the complete clinical picture of cerebrospinal meningitis, but the lumbar puncture fluid was almost pure blood at three punctures. There had been no trauma, but serologic tests were positive, and under treatment as for syphilis complete recovery promptly followed. Six weeks after the first symptoms the spinal fluid was normal. Extreme ophthalmoplegia was one of the early symptoms.

ACUTE SYPHILIS OF THE LUNG. ARY MIRANDA, *Brazil-Medico* **34**:675 (Oct. 9) 1920.

Nothing but the absence of tubercle bacilli in the sputum contradicted the assumption of an acute tuberculous process in the left lung of the man of 19 with rapid destruction of tissue, extreme weakness, sweats, dyspnea and profuse expectoration. There was no history of acquired syphilis, but inherited syphilis could not be absolutely excluded, and under treatment for syphilis clinical recovery promptly followed. The Wassermann test had been constantly negative but veered transiently to positive during the course of treatment.

SKIN DISEASES AND SYPHILIS IN 1920. H. GOUGEROT, *Médecine*, Paris **2**:85 (Nov.) 1920.

In the course of this long review Gougerot remarks that there seems to be increasing agreement as to the wisdom of large progressive doses in primary syphilis. Milian gives from 0.3 to 0.9 gm. or even 1.2 of neo-arsphenamin in the primary phase. Leredde in the second and third phases begins with small doses, 0.1, increasing to 0.9. With syphilitic disease in the nervous system, kidneys or aorta, the doses recommended are between 0.1 and 0.3. The advantage of associating mercury with the arsenicals is admitted more and more. "The arsenical attacks, but the mercury brings up the reinforcements to hold what has been gained." As to mishaps with the arsphenamins, Gougerot thinks that damage of the organ by the drug and damage by the syphilis both cooperate. Abadie declares that in rebellious cases treatment should be kept up with mercuric cyanid by the vein every second day, from 0.01 to 0.02 gm., for one, two or three years if necessary, and reports success beyond all hopes in certain cases by this means. Gougerot presents the arguments for and against there being more than one type of spirochete, inclining to the negative view himself. He mentions parenthetically a special calendar he gives to his syphilitic patients.

HOW TO CURE THE SYPHILITIC. L. QUEYRAT and M. PINARD, *Médecine*, Paris **2**:101 (Nov.) 1920.

Queyrat and Pinard laud the method of attacking syphilis at its beginning by striking hard, in six day doses, beginning with 0.15 gm. of arsphenamin and reaching 0.6 by the eighth injection.

INHERITED SYPHILIS AND DENTITION. R. SABOURAUD, *Médecine*, Paris **2**:105 (Nov.) 1920.

Sabouraud cautions against overlooking malformations of the teeth as they may seem normal on casual inspection unless they are counted, and the jaw examined. These signs of the inherited taint are particularly instructive as they are permanent.

SYPHILIS OF THE NERVOUS SYSTEM. J. A. SICARD, *Médecine*, Paris **2:111** (Nov.) 1920.

Sicard reiterates the great value of small, repeated doses of neo-arsphenamin and iodid, kept up every day or second day by both the subcutaneous and the intravenous route. The family can be trained to do this. Five of his patients with typical general paresis have resumed their place in the family if not in business, and the improvement has persisted for three years. Three times a year each is given a course of small repeated doses to a total of from 7 to 10 gm. Some have taken up to 70 gm. of neo-arsphenamin during the three years. His opinion of intraspinal injection is that it is deluding, and does not deserve the praise given it in America and in Spain, while experience has convinced him of its dangers.

JAUNDICE AND ARSPHENAMIN. G. MILIAN, *Médecine*, Paris **2:113** (Nov.) 1920.

Milian says that he at first believed the jaundice was the work of the arsenicals but three years of study have convinced him of his error, and he now declares that the syphilis itself is responsible for it, as also for the ocular, facial or other paralysis sometimes noted. These phenomena are observed only by those giving too timid doses; thirty such cases have been sent him in the last eighteen months, and in every instance the dosage had been too weak or the technic defective. All were treated vigorously with the arsenicals and the cure was soon complete; if the drug were responsible, it would be an unheard of thing to cure a manifestation of poison by giving more of the poison.

ARSPHENAMIN ERYTHRODERMIA. L. BRIN, *Médecine*, Paris **2:117** (Nov.) 1920.

Brin mentions that the extensive and desquamating erythrodermia appeared after from seven to twenty injections of neo-arsphenamin. In such cases there had usually been up to 5 to 10 gm. injected during the current course of the treatment. The drug should be stopped at once, nothing but milk allowed for a few days, and then a milk-vegetable diet, rinsing out the intestines thoroughly with boiled water. All active local treatment should be avoided.

PATHOGENESIS OF NEURORECURRENCE. H. GOUGEROT, *Médecine*, Paris **2:119** (Nov.) 1920.

Gougerot explains the neurorecurrences and the symptoms developing in viscera, after arsenical treatment, as a combination of toxic manifestations and flaring up of the syphilis. The syphilis has become modified by the treatment until it is tertiarized, the lesions assuming the destructive character of the spontaneous tertiary phase. If the toxic element predominates, further arsenical treatment can do only harm, but, if the visceral lesions outshadow them, then further arsenical treatment will usually cure.

ELIMINATION OF ARSPHENAMINS. M. POMARET, *Médecine*, Paris **2:123** (Nov.) 1920.

Pomaret's research has confirmed that more of the arsphenamin is eliminated by the intestines than by the kidney after intravenous injection. The bile from a dog with a bile fistula showed constantly more than 1 cg. in 5 c.c. of bile, while 15 c.c. of the urine contained only fractions of a milligram. As the amount of bile secreted in the twenty-four hours is about equal to that of the urine, the importance of this mode of elimination is obvious. Similar experiments on a rabbit gave analogous findings. Jeanselme has published a

case in which 1 cg. arsenic was found in the vomit from five to eight hours after injection of 0.6 gm. of arsphenamin. We know also that the hair, the skin, etc., retain arsenic in considerable amounts. Elimination seems to be slower after intramuscular injection. Simultaneous mercurial treatment retards elimination somewhat.

EARLY DIAGNOSIS OF SYPHILIS. L. SPILLMANN, *Médecine*, Paris **2:126** (Nov.) 1920.

Spillmann extols the important aid which the pharmacist can render in the organized fight against syphilis by warning the customer to seek a proper diagnosis at once. He cites the resolution recently adopted by the Nancy Medical Society urging pharmacists consulted by persons with genital lesions to impress on them the extreme urgency of their being examined by a physician before selling them remedies which may waste precious time.

ABORTION OF SYPHILIS. LÉVY-BING and GERBAY, *Médecine*, Paris **2:130** (Nov.) 1920.

Lévy-Bing and Gerbay discovered that the Bordet-Wassermann reaction appeared always after a certain interval from the hour of contagion. If abortive treatment is pushed before this date it has every prospect for success, but after this date, treatment may retard the appearance of the positive reaction but does not prevent its becoming positive sooner or later. This interval is thirty-seven days long, counting from the hour of infection. Then comes a period of eight days during which the outcome is dubious, but after the forty-fifth day no treatment will ward off a positive reaction. Hence, they conclude, abortive treatment cannot be counted on to be effectual after the thirty-seventh day.

TREATMENT DURING INCUBATION OF SYPHILIS. A. TZANCK, *Médecine*, Paris **2:132** (Nov.) 1920.
132 (Nov.) 1920.

Tzanck insists that the spirochete should be the call to arms; we must not wait for a positive Wassermann reaction.

NEO-ARSPHENAMIN BY THE VEIN FOR SYPHILITIC INFANTS. G. BLECHMANN, *Médecine*, Paris **2:137** (Nov.) 1920.

Blechmann points to the mounting tide of infants with inherited syphilis, and the greater recognition of the ever widening sphere of its evil influence. We must attack it at once and strike hard, profiting by the efficacy of the arsenicals in addition to mercury. He begins with less than a centigram per kilogram, increasing to 0.015 or 0.02 gm. every sixth or seventh day, by the vein, in series of from five to ten injections, with suspensions for a month or two.

Society Transactions

SOCIEDAD ESPANOLA DE DERMATOLOGIA Y SIFILIOGRAFIA

Inaugural Meeting of the Year 1920-1921, Oct. 15, 1920

DR. AZUA, *Presiding*

SYPHILITIC MENINGITIS D'EMBLEE. DR. PORTILLA.

I wish to report the case of a young man, aged 25, who had occult syphilis, without ever having had chancre or any other manifestations. The parents were apparently healthy; the mother had been pregnant ten times, labor always being normal. All the children were healthy and the father had a negative history. Last March the patient began to suffer with meningitis, accompanied by symptoms of insanity, hemiparesis and aphasia due to involvement of the motor zone. Syphilis was diagnosed by exclusion, in spite of the negative blood Wassermann reaction, and the diagnosis was confirmed by the examination of the cerebrospinal fluid and the success obtained with the specific treatment. My conclusions from this case are: 1. We must keep syphilis in mind when no other disease is apparent, in spite of a negative history. 2. The Wassermann test must be appreciated at its true value and should be neither omitted nor abused. 3. All praise is due to those who introduced mercury and, above all, arsphenamin, in human therapeutics.

EPITHELIOMA ON THE BACK OF THE RIGHT HAND. DR. FORNS.

A woman, aged 76 years, two years ago developed a lesion on the dorsal part of the hand. Curettage was performed in her native town, but it did not destroy the lesion. At present it is an epithelioma of the *ulcus rodens* type, larger than a dollar in size. It is closely attached to the deeper tissue, and there are infarcts in the epitrochlear region and some suspicious signs in the axillary region. I report the case, first, on account of its rare location and, second, on account of the therapeutic problem. We must remember that it is an epithelioma with gland involvement, closely attached to the deeper tissues. We should not forget how seriously epitheliomas in this region are considered by most authorities. Surgical eradication would leave the patient with an unsightly defect, due to the large amount of tissue destroyed. This loss would be difficult to replace, practically amounting to amputation of the hand, which should be avoided by all means. Therefore, we suggest epitrochlear and axillary cleaning, followed by the application of radium to the epithelioma.

DISCUSSION

DR. SAINZ DE AJA: Epitheliomas on the hand are a medical snare. It was once believed that the smaller ones and those free from glandular involvement healed easily. Experience has shown, however, that even these are serious. This is confirmed by this case, its seriousness being enhanced by its glandular involvement. I think that the best procedure is that suggested by Dr. Forn's.

SPOROTRICHOSIS. DR. BARRIO DE MEDINA.

I wish to discuss first the alleged case of sporotrichosis reported by Drs. Gimeno and Criado last year, which afterward was referred to us, the patient entering Dr. Sainz de Aja's service in the Hospital de San Juan de Dios. As may be remembered, the patient was a woman with multiple foci in the skin of the left cheek, right third metacarpal and fourth finger and about the left breast. They were considered sporotrichosis nodules and abscesses, both because of their clinical appearance and the patient's history, as she apparently had an initial chancre in the right thenar region. When the case was last discussed she had been submitted to iodid treatment by Dr. Gimeno, but in view of the improvement of the lesions, there was yet some question as to whether it was sporotrichosis or whether a sufficient amount of iodid had been taken. The patient was in this condition when she came to us. We have given her in one month twenty-five intravenous injections of potassium iodid of 1 to 2 gm. each, making a total of 43 gm., in addition to 90 gm. by mouth. Locally we treated the lesions with iodine-xylol. Even with this treatment the lesions did not improve. This would have been sufficient to disprove the diagnosis of sporotrichosis, but in addition Dr. Arcaute was unable to grow the *Sporotrichum*, and biopsy material showed definite tuberculosis infection. The plan of treatment was therefore changed completely. When still under antituberculosis treatment, she had to be transferred to the maternity ward. When discharged there, we expect her return to continue the treatment.

The other case is that of a boy who had gonorrhea, also reported last year by Dr. Sainz de Aja. He was wounded in the sole. This was followed by infarct of the axillary glands. The Wassermann reaction was positive, and when he was being treated for syphilis, some peri-osteal foci developed in the frontal region, the superciliary arches and the sternal region. Although the lesions and their location seemed specific, both their appearance while he was under treatment and the initial lesion suggested sporotrichosis. The antisyphilitic treatment was completed with twelve injections of benzoate of mercury, one of gray oil and five of neo-arsphenamin. While he was still under this treatment, the periostic foci near the sternum grew much worse. Therefore we placed him exclusively under a treatment of 3 gm. of sodium iodid daily by mouth and intravenous injections of sodium iodid; he received altogether 34 gm. intravenously and 190 gm. orally in about two months. The striking feature of the case is that the patient did not improve at all with the drug and Dr. Arcaute, who had collected some pus from the sternal focus, reported that he had grown the *Sporotrichum* from it. Then the patient began to complain that he was gradually losing the power of vision in his left eye. We referred him to an eye specialist, who suggested an examination of the frontal sinuses. Dr. Hinojar was then consulted, who advised an immediate operation, the patient being transferred for this purpose to the General Hospital. We regret having lost track of him as Dr. Hinojar told me some days ago that they had to discharge the patient because he broke the rules.

DISCUSSION

DR. GIMENO: I want to explain my handling of the first case. Iodid was administered and as the search for the *Sporotrichum* was negative, I suspected it was not sporotrichosis. The only thing left undone was a biopsy to clear up the diagnosis.

DR. SAINZ DE AJA: In my opinion the reason the second patient did not improve, although he had sporotrichosis, is that he was syphilitic. Since he suffered from osteomyelitis, there was probably also some sequestrum. As is well known, these patients do not recover entirely until the sequestrums have been taken out.

NEW YORK DERMATOLOGICAL SOCIETY

Regular Meeting, Oct. 26, 1920

J. M. WINFIELD, M.D., *President*

PRURIGO. Presented by DR. WHITEHOUSE.

The patient was presented merely as a matter of interest, on account of the rarity of the condition. It seemed to be a clearcut case of the old prurigo of Hebra. The patient, Anna M., aged 13 years, was born in this country. She had suffered from the disease since she was 17 months old. She presented a very definite case of Hebra's prurigo, on the arms, legs, body, and on the face. The papules, which at first appeared to be the color of the skin, later became inflammatory. The flexor surfaces were not involved. The axillary and inguinal adenopathy was very marked. Itching was intense. Treatment had been without avail; the only thing that gave any relief was baths of an antiseptic of the chlorin type. The lesions were more inflammatory than in some of the cases seen, but a notable point was the freedom of the flexor surfaces. The diagnosis was accepted without dissent.

LYMPHOSARCOMA. Presented by DR. CLARKE.

The patient, a police officer who had been shown before the Society in 1917, had a large lymphosarcoma, about the size of the palm, on his head. The case was referred by Dr. Eugene Poole, and at the time of presentation the members were unanimous in diagnosing the case as sarcoma. The patient was treated with a massive dose of roentgen-ray, resulting in a bad roentgen-ray burn of the second degree, but that cleared up and when presented he showed an excellent result of the treatment.

MELANOTIC SARCOMA TREATED BY ROENTGEN-RAY. Presented by DR. CLARKE.

The patient had been presented before the Society in the spring, after a massive dose of radium for melanotic sarcoma. At that time, she was presented to get the opinion of the members as to whether she should have further exposures or submit to surgical treatment. Some of the men had seemed to think that a portion of the malignant tumor still remained, but Dr. MacKee thought it was simply the radium burn. It was thought best to wait and see what happened. Finally, all the remaining black spots disappeared, leaving a frank roentgen-ray burn. The entire piece of tissue was excised and carefully examined, and the pathologist reported that nothing malignant was present. Then the lesion was skin-grafted. The patient was presented in May of last year. At present, there is no glandular enlargement anywhere. There was some keloid, but that seemed to be diminishing rather than increas-

ing in size. Prior to the treatment, the lesion had existed for a long time. At first, it was about the size of a split pea, and then it began to increase rapidly until it was about the size of a half dollar.

DISCUSSION

DR. TRIMBLE said that he had seen the patient with the melanotic sarcoma before, and congratulated Dr. Clarke on the results. He had been wondering, however, whether the lesion would not have healed better without the skin graft.

DR. HIGHMAN said that in reporting cases of this sort in which the histological diagnosis is not made, mention should be made of that fact.

DR. CLARKE said that he believed radium burns healed up more kindly than roentgen-ray burns. He had wanted to excise it on that account, for he wanted to get the whole area. It was minutely examined, for he wanted to see whether anything could be found, for Drs. Whitehouse and Fordyce believed that there was still some malignant disease remaining when the patient was presented before. He was not seeking a cosmetic effect at the time.

RADIODERMATITIS. Presented by DR. HOWARD FOX.

R. C., a woman, aged 32 years, born in the United States, and a stenographer by occupation, six years before had consulted a physician in a neighboring city for an extensive hypertrichosis of the face. She stated that she had received from fifteen to eighteen roentgen-ray treatments in the course of three weeks. This was followed by a severe "burn with blisters," and at the end of a month the skin had peeled, leaving permanent disfiguration.

She now presented over the bearded region the results of a severe radiodermatitis, consisting of distinct pigmentation, telangiectasia and whitish superficial scars. No keratoses were present. The lesions were most distinct on the cheeks, chin and neck, the upper lip being only slightly affected. The patient was shown to emphasize the inadvisability of treating hypertrichosis with roentgen ray. The most careful treatment by measured doses has its dangers, while in this particular case it seemed probable that the operator lacked the necessary knowledge to use roentgen ray properly.

DISCUSSION

DR. WISE, replying to a query from Dr. Fox, said that he himself had used the Kromayer lamp in roentgen-ray telangiectasia but the results were very poor. He used radium in roentgen-ray keratoses with good results, but did not think one could accomplish very much with the Kromayer lamp in a case like this one as far as the vascular lesions were concerned.

DR. CLARKE said that he had had some success in cases of telangiectasia following roentgen-ray burns by the use of radium, and he recommended its application in this particular case. He would be rather skeptical of the effect of the Kromayer lamp in such a case. It could only be used with a blue filter and pressure and very prolonged exposure. The patient showed a tendency to freckle, and with a prolonged exposure the chances were that she would have freckles from it. He would treat such cases with the electric needle, and whenever possible radium. He thought the condition could be very much improved. Replying to a query of Dr. Wise, Dr. Clarke said that in many cases he had been able to make a dilated vessel close up with the needle.

DR. HIGHMAN said that he did not see how it was possible for radium to produce that effect.

DR. CLARKE said that he had been able to do that by filtering the radium with 0.75 mm. to 1 mm. of lead to get a very penetrating exposure.

DR. HIGHMAN said that the vessels in nevi are neoplastic in their nature and represent a constantly proliferating process. For that reason they are influenced by radium, though not so much by the roentgen rays as by the beta rays. Telangiectasia produced by the roentgen rays has an entirely different origin. It is due to the fact that elastic tissue is destroyed, which eliminates vascular tone, so that the vessels naturally dilate under the increased pressure of the circulating blood, and being scarred vessels they do not respond to radium.

LICHEN OBTUSUS. Presented by DR. HIGHMAN.

The patient, who was about 19 years of age, presented very curious lesions on the thigh, which began to appear six years before on the left thigh. Others developed later, and one appeared on the forearm. The itching had been very severe some years before, but had ceased. The lesions were regarded as warts. The patient had been carefully examined for lesions on the mucosa, but none were found. The treatment had consisted of mercuric chlorid, internally, and salicylated alcohol, externally.

DISCUSSION

DR. WHITEHOUSE said that it did not seem fair to criticize a diagnosis when one could not make a better one, but he could not subscribe to the diagnosis of lichen in this case. No doubt it was hypertrophic, but the lesions were so changed by the treatment that it was difficult to say what their nature was. It would be desirable to investigate the case by biopsy to see whether there was any resemblance to the conditions found in tuberculosis verrucosa. The isolated lesion on the back of the thigh that had not been touched looked like tuberculosis verrucosa.

DR. CLARKE said he could not make a diagnosis, but would like to know whether there was anything in the history to indicate that the patient had been taking bromid.

DR. HOWARD FOX said it was difficult to make a diagnosis in a case that had been so disguised by treatment. Some of the lesions suggested lymphangioma circumscriptum, and as had been said others suggested bromid lesions. It would seem that the diagnosis would have to be settled by the microscope.

DR. WISE said that he would accept the diagnosis as presented—lichen planus verrucosus.

DR. HIGHMAN said that except for the lesion on the back of the thigh he questioned whether he would tonight have made the diagnosis submitted. When the patient was first seen, the lesions on the left thigh looked like lichen hypertrophicus and those on the abdomen were typical lichen papules. The other possibility that had been raised could be ruled out for two reasons: The boy had had the lesions for from four to six years, which would rule out a bromid eruption; and the fact that the lesions were not vesicular would rule out the possibility that Dr. Fox mentioned. Other possibilities—warts, different benign tumors, epithelioma—were not considered. He had wished to make a biopsy, but the boy was timid about it. The father, however, had consented to have it done, and a report would be submitted at the next meeting.

LICHEN PLANUS OR NEVUS UNIUS LATERALIS? Presented by DR. WISE for DR. FORDYCE.

A young woman, aged 26 years, presented lesions on the left arm and leg which were of fourteen years' duration. Slight itching was said to be present. The diagnosis seemed to lie between atrophic lichen planus and nevus linearis, but the biopsy did not show either. The lesions consisted of atrophic, small, pigmented papular lesions, arranged in linear fashion along the arm and leg.

DISCUSSION

DR. HIGHMAN did not know what to say about it. If it were lichen planus, it would be of the atrophic pigmented variety, but the atrophic variety is not usually pigmented. And if it was a nevus he did not know why it should itch and atrophy. He was at a loss to classify it.

DR. TRIMBLE said he would not hesitate to make a diagnosis of nevus in the case. The fact that there were some flat papules would not change his opinion.

DR. HOWARD FOX said that he had a patient under treatment with a warty linear lesion extending down the back of the thigh from the buttock. As it had existed from birth, he felt sure that it was a nevus in spite of the fact that the patient had complained a good deal of itching.

DR. CLARKE said he could not reconcile a case of linear nevus with such extreme itching, the atrophy and the rather diffuse distribution. He was inclined to a diagnosis of atrophic lichen planus.

DR. WISE said that a biopsy report would be submitted at the next meeting.

VERRUCA. Presented by DR. TRIMBLE.

The patient, a Porto Rican, aged 36 years, with a negative family and personal history, presented a condition which began on the dorsum of the left foot twenty-five years before as small verrucous lesions. At that time, the patient was working barefooted in the tobacco and sugar fields of Porto Rico. The lesions gradually enlarged in size, and at the end of six months spread to the dorsum of the right foot, and had since continued to enlarge and spread until they attained the extent exhibited. A few years before, after scratching the feet and getting blood on the fingers, the patient noticed lesions appearing on the fingers.

The condition presented consisted of discrete and confluent brownish verrucous lesions, varying in size from that of a small pea to several inches in diameter, covering the feet and stretching up the leg, and also appearing on the fingers. The Wassermann reaction was negative. The pathologic report was verruca.

DISCUSSION

DR. WHITEHOUSE agreed with the diagnosis.

DR. CLARKE said that he had seen the patient before he received any treatment, and agreed with the diagnosis. The lesions when treated with salicylic acid applications had improved more than those treated with roentgen ray. He expressed doubt whether a good result could be obtained with the lesions unless they were cleared of the crusts or scales before the roentgen-ray treatment was applied.

DR. WINFIELD agreed with Dr. Clarke that the foot that received the salicylic acid looked better, and also agreed that if the lesions were first curetted and then the roentgen-ray applied a cure would probably result.

DR. TRIMBLE said that the lesions had received no treatment prior to being treated with the roentgen ray. They were not curetted, but were soft when they were irradiated.

LESIONS RESULTING FROM MORPHIN HYPODERMICS. Presented by DR. WISE for DR. FORDYCE.

A young woman, aged 27, who for six years had been addicted to the morphin habit, presented lesions which covered her arms where the injections had been made. There were the characteristic hard bluish masses, a half centimeter in diameter, some discharging pus and serum.

RECURRENT (STREPTOCOCCIC) DERMATITIS OF FACE. Presented by DR. HOWARD FOX.

W. H. K., a man 41 years of age, born in the United States, an administrative assistant in the U. S. Public Health Service, six months before had suffered from an eruption similar to the present one, lasting five days. A second attack, lasting seven days, occurred three months later. The present attack appeared five days before, and was now rapidly subsiding. When seen on the second day, he presented a dermatitis about the eyes, nose, and cheeks, more severe on the left side. The affected area was red, hot and edematous, but showed no vesiculation or sharp demarcation characteristic of erysipelas. In this, as in previous attacks, he complained of slight constitutional symptoms consisting of anorexia and headache. There was also a slight rise of temperature. He complained of a burning sensation of the skin but no itching. He had suffered from a severe attack of poison ivy dermatitis six years before. Previous to each of these attacks, he had not been exposed to his knowledge to any cutaneous irritant. He had suffered a good deal from nasal catarrh and from indigestion. Examination of the nose revealed no gross lesions. Examination of the swabs from the nasal passages, after irrigation with sterile saline, were made at the Marine Hospital (Stapleton). The result was as follows: "On Loeffler's blood serum a profuse growth within twenty hours, which on smear preparation showed a gram-positive micrococcus. On transplanting to blood dextrose broth, a hanging drop showed a micrococcus with no definite morphology similar to that of streptococcus. Culturally, organism isolated was *Micrococcus aureus* of low virulence."

DISCUSSION

DR. HIGHMAN said the thing to do in such a case was to get the serum from the lesions during an acute attack, make a vaccine and treat the patient.

DR. WISE said that he had very little personal experience in such cases, but that he had seen patients treated by others, and that the procedure outlined was the same as that referred to by Dr. Highman.

DR. FOX replied that nothing abnormal had been found by the rhinologist at the Marine Hospital. Dr. Fox had recently presented before another society a patient who suffered from a permanent elephantiasic swelling below the eyes. An attempt had been made by one of the Public Health surgeons to obtain fluid for culture by puncturing the swollen tissue, but without success.

DR. WINFIELD said he had seen several cases of this condition and had always found some lesion about the nose which seemed to light up the attack. He believed the stock vaccines would do as well as the autogenous vaccines.

DR. FOX replied that at the hospital they stated there was no visible lesion. At the Academy Section last winter he had presented a man with frequently recurring edema below the eye, and some of the physicians in the Public Health Service tried this procedure but were unable to get enough fluid to make a culture.

EPIDERMOLYSIS BULLOSA. Presented by DR. WISE for DR. FORDYCE.

A woman, aged 27 years, had had the present condition since last March. She was married and had one child. For the last eight months she had had lesions similar to those exhibited. The lesions consisted of scattered vesicles and small bullae on the face, neck and hands. They often arose on striking the skin by accident or otherwise. It seemed to be a case of epidermolysis bullosa of the nonhereditary type. No other members of the family showed any similar lesions. The patient also presented little miliary epidermal cysts on the shells of her ears and on the fingers. The outer surface of the elbow regions exhibited the characteristic atrophic scarring, resulting from previous lesions.

DISCUSSION

DR. HIGHMAN said that he had not a clear perception of the case. It would seem that if it were epidermolysis it would be possible to elicit Nikolsky's sign. The lesions on the ear looked like ordinary dermatitis in that location. He did not understand what was meant by the term epidermolysis bullosa acquisita.

PARAPSORIASIS GUTTATA. Presented by DR. WISE for DR. FORDYCE.

A boy, aged 12 years, born in Russia, had been troubled with the lesions for twelve months. He had been presented before the Academy of Medicine, at which time he showed a great number of small, pinkish macules, isolated and confluent, some of them slightly scaly. He had had a considerable number of treatments, but according to his parents they had had absolutely no effect on the condition. The impression was that he had psoriasis. Later, on account of the type of the eruption, and its peculiar resistance to treatment, a diagnosis of parapsoriasis guttata was made.

DISCUSSION

DR. FOX and DR. TRIMBLE agreed with the diagnosis.

DR. WISE said that he had treated a patient referred by Dr. Wallhauser with roentgen rays and the eruption cleared up entirely. While the patient was under treatment, however, a new crop of the lesions appeared in the interval between two weekly applications of the rays.

DR. HIGHMAN said that in one of the issues of a German journal a physician had related his experience with parapsoriasis and purports to have cured all his patients by injections of one-tenth grain of pilocarpin every other day. The patients improved after two or three injections and were cured in a few weeks.

ACRODERMATITIS CHRONICA ATROPHICANS WITH FIBROTIC TUMORS. Presented by DR. WISE for DR. FORDYCE.

A married woman, aged 45 years, born in Russia, had had the lesions presented for ten years. The history given was rather vague, but it was gathered that the trouble began with a feeling of coldness in the feet and the skin became "hard." The trouble had traveled up toward the groin. She also presented distinct fibrotic nodules associated with atrophy on both elbows—the so-called ulnar band—and the characteristic cutaneous atrophy of both legs.

The diagnosis was accepted without dissent.

DISCUSSION

DR. HIGHMAN said that if therapeutic observations were of any interest, he could tell of a similar case with band-like lesions, and on the homeopathic principle of *similia similibus curanter* he had used the roentgen rays which was followed by a very rapid limbering of the tissue. Whether or not that was simply a coincidence he could not say.

PHENOLPHTHALEIN ERUPTION. Presented by DR. WISE for DR. FORDYCE.

E. A., a married woman, aged 25 years, presented herself at the Vanderbilt Clinic with a fresh outbreak of an eruption which had recurred, at intervals of from one to four weeks, during the past three years. The forehead, face, shoulders, axillae, arms and thighs, showed a number of macular and urticarial lesions from 1 to 3 cm. in diameter, bluish red, and suggesting erythema perstans. Several days later, when the eruption had subsided, she was given two 5-grain tablets of phenolphthalein, and the following day many of the spots had appeared in all their intensity.

DISCUSSION

DR. HOWARD FOX said that phenolphthalein seemed to produce an eruption that was more or less characteristic. This consisted of well defined, round or oval erythematous or urticaria-like coin-sized lesions, followed by rather persistent pigmentation. He had had a similar case due to an ingestion of exlax (a patent preparation containing phenolphthalein).

DR. WINFIELD said that he had seen a somewhat similar eruption from antipyrin. From this coal tar preparation, however, the patches were more erythematous and not purpuric. The erythematous patches often left a brown stain which was more or less chronic.

LICHEN PLANUS. Presented by DR. WISE for DR. FORDYCE.

G. V., a sturdy fireman, aged 28 years, presented the typical lesions of lichen planus on his lips and chin, and on the backs of his hands. The noteworthy point was the extensive involvement of the vermilion portion of the lips and the complete absence of lesions on the mucous surface of the lips and interior of the mouth. The lesions on the lips had been present for seven weeks; those on the hands for one week.

CASE FOR DIAGNOSIS (PAPULONECROTIC TUBERCULID?). Presented by DR. WISE for DR. FORDYCE.

H. R., aged 57 years, a salesman of Russian birth, had lived in America eight years, and gave a negative family history. His face, scalp and extremities bore closely crowded lesions in various stages of development, ranging from $\frac{1}{8}$ to $\frac{1}{4}$ inch in diameter. There were many violaceous papules, more or less firm to the touch, some capped with crusts whose removal disclosed the presence of dry, necrotic centers. Many older lesions, dry, atrophic and pitted, were interspersed with these. The lesions on the face resembled acnitis. The patient said the eruption had been present only for the last fifteen months. His health was good otherwise, but he complained of severe pruritus of the affected parts. A biopsy was obtained, but the histologic examination did not show it to be papulonecrotic tuberculid.

DISCUSSION

DR. HIGHMAN said it was either papulonecrotic tuberculid or prurigo, and he could not see any diagnostic evidence of the former.

DR. HOWARD FOX said the important point to decide was whether the condition was an inflammation or a granuloma. The evidences of intense itching and the absence of pitted scars (as in a papulonecrotic granuloma) spoke strongly in favor of an inflammatory condition. It was of less importance to decide whether the disease should be classed as a prurigo or a dermatitis herpetiformis.

DR. WHITEHOUSE agreed with Dr. Fox that the lesions on the forehead were not scar-forming lesions. In consequence of the intense itching and grouping of lesions, it impressed him as a peculiar type of Duhring's disease, or some kind of inflammatory disease.

DR. WISE, replying to a query from Dr. Lane, said that he did not think the lesions on the forehead itched as did those on the hands. He would submit a biopsy report at the next meeting.

DR. WINFIELD said that he saw nothing in the case to make him think of dermatitis herpetiformis.

UNUSUAL TYPE OF SYPHILODERM: REPORT OF CASE. Presented by DR. HIGHMAN.

A man, aged 50 years, had a pruriginous annular group of granulomatous lesions on the scrotum and elsewhere. There were about eight lesions, ring shaped, plaque shaped or papular, deeply set in the subcutis, varying in size from 0.25 to 2 cm. in diameter, violaceous and of a hard but elastic consistency. Clinically, they suggested granuloma, a diagnosis substantiated microscopically, and made despite the localization. Severe itching was complained of. Syphilis was denied.

Under roentgen-ray treatment no improvement was evident, and the question of syphilis was again raised. Although the Wassermann test was negative, antisppecific treatment was begun, and within forty-eight hours after the first arsphenamin injection, the lesions had shrunk to one-half their original volume, the itching having stopped at once.

In this connection it must be added that the right index finger was swollen. Radiographic examination showed the bones to be normal. Thus the finger con-

dition represented an infiltrated edema of the soft parts. This, too, healed under specific treatment.

The patient was shown because of these points: (1) itching relieved by antisyphilitic treatment, (2) the rare character of the lesions, and (3) the weak serum reaction.

SKIN SHEDDING (KERATOLYSIS EXFOLIATIVA CONGENITA). REPORT OF CASE. Presented by DR. HOWARD FOX.

Mrs. L. E. G., aged 28 years, born in Texas, was seen in consultation eight months before. She stated that during her entire life she had suffered from peeling of the skin in flakes similar to those of scarlet fever. The desquamation affected the entire body and was never associated with redness or any subjective symptoms. At intervals of a week or less the skin shedding would become active. No one else in her family had suffered from a similar condition. She had always enjoyed good health and had no theory to offer regarding the cause of her affection. The desquamation was not affected by the menstrual periods and did not vary during the different seasons of the year. It was not affected by the use of oily applications. Her chief complaint was the embarrassment caused by the appearance of the skin at times.

On examination she showed a slight, flaky desquamation of the chest of a scarlatiniform type. There were no inflammatory changes, with the exception of a definite factitious urticaria. There was no evidence of ichthyosis, her skin in general being remarkably soft and smooth. There were no abnormalities of the hair and nails. She was well nourished and appeared to be in the best of health living an outdoor life of leisure.

DERMATITIS VENENATA FROM ORIENTAL CASHEW NUT. REPORT OF CASE. Presented by DR. HOWARD FOX.

Miss M. L., aged 32 years, was a laboratory worker in the U. S. Department of Agriculture. She was born in the United States, but until lately had lived in Germany for fifteen years. During the last four months she had been working in the laboratory where she was constantly handling various plants. She was first seen on September 11, when she presented a severe generalized dermatitis similar to that from rhus poisoning. This was most marked on the face and upper extremities and consisted of a profuse vesicular and itchy eruption, associated with extreme edema, the eyes being closed and the features unrecognizable. The patient was confined to her bed. The eruption gradually subsided but the edema did not disappear when treated with cold compresses or boracic acid as fast as is usually noted in rhus dermatitis. At the end of three weeks, the eruption had disappeared except for flaky desquamation of the hands. This was entirely well about two weeks later.

The eruption appeared on the day after she had handled specimens of Oriental Cashew nut (*Anacardium orientale*), the fruit of a tall tree of India. While she was cutting several nuts and making microscopic sections for about an hour and a half, some of the juice of the mesocarp came in contact with her hands, staining them a blackish hue. Two other workers, a man and a woman in the same laboratory, handled the same nuts and on the following day presented an eruption on the face and hands. The man, who had handled the specimens longer than the woman, and whose hands had become slightly blackened, was said to have had a more severe eruption. One other laboratory assistant had touched the nuts without ill effect, and the same was true of the helper who washed the instruments which had been used in making sections.

As a possible cause of the dermatitis, it should be said that the patient had been in the Catskill Mountains five days before the eruption appeared. She did not, however, handle any poison ivy leaves. She had never previously suffered from rhus poisoning to her knowledge, though it must be said that during the greater part of her adult life she had lived in Germany.

The patient appeared to be susceptible to irritation from plants, as on a previous occasion (end of June) she had handled sanguinaris powder and on the following day an eruption had appeared on the face, neck and chest, and between the fingers. It was red and showed "blisters," and lasted ten days. This attack also followed a short walk in the country (three days previously) though she did not, as far as she was aware, come in contact with poison ivy. Very recently she had again suffered from a slight eruption on the wrists, on the day after she had handled pistachio nuts. This lasted only two days. On this occasion she had immediately used alcohol and zinc oxid ointment.

The oriental cashew nut, which was presumably the cause of the dermatitis in this case, is to be distinguished from the cashew nut which is a native of tropical America (*Anacardium occidentale*). The oriental, like the native species, is known to be a cutaneous irritant.

DISCUSSION

DR. WISE inquired concerning the five days' incubation period of poison ivy.

DR. FOX replied that the eruption came on very suddenly after the exposure. He had never seen a case in which the incubation period lasted five days.

DR. WINFIELD said that he had had personal experience. On some occasions the eruption did not develop for ten days to two weeks after exposure, although there was considerable itching before the eruption appeared.

DR. WISE said that he had seen a case in a clinic on a Monday in a man who stated that he had been in the woods on the preceding day, Sunday, that is, seven days previously.

DR. HIGHMAN told of a patient seen on a Wednesday, the exposure having occurred on the previous Sunday, or four days earlier.

PHILADELPHIA DERMATOLOGICAL SOCIETY

Regular Monthly Meeting, Nov. 8, 1920

MILTON B. HARTZELL, M.D., *Presiding*

MYCOSIS FUNGOIDES. Presented by DR. HARTZELL.

A printer, 50 years old, had a universal dermatitis for over two years. In most situations it exhibited a smooth, shiny red infiltration, itchy and slightly scaly, the latter condition being most marked on the palms. Significant features of the disease were numerous eruptions on the trunk in the form of scores of flat, infiltrated, slightly elevated, scaly areas ranging from the size of a pea to that of a fingernail. These tumors had been present for the past four months. They were most abundant on the upper trunk, both anteriorly and posteriorly. Adenopathy was marked; the inguinal and axillary glands stood out in relief. No laboratory findings were reported. A moderate degree of conjunctivitis was present.

DISCUSSION

DR. SCHAMBERG agreed with the diagnosis and regretted that no blood count had been made on account of the resemblance of this disease to leukemia of the skin.

XERODERMA PIGMENTOSUM. Presented by DR. SCHAMBERG.

This boy of 13 had been under observation for eight years. During this time several carcinomas were removed from his face by means of the actual cautery. Two years ago a mushroom-like growth of myxomatous character was excised from the scalp. Two brothers had the disease. The patient exhibited extreme photophobia due to corneal ulceration. Freckle-like lesions were present on the conjunctiva and in large numbers on the skin. Several carcinomatous growths were present, the largest being near the right corner of the mouth. The patient's mental condition had improved, and he was not as depressed as formerly.

The action of the sun on these cases might be likened to that of the roentgen-ray bulb, but the use of the latter was justified in treating localized areas of this disease.

A CASE FOR DIAGNOSIS. Presented by DRs. MUNSON and STRAUSS.

A white woman, aged 25, married, had a more or less generalized itchy eruption, which had been present for four and a half years. The lesions were transitory, remaining for from a week to a month. Recently pigmentation had appeared on the parts most affected—the neck, upper chest, the inner side of the upper arm, abdomen and groins. The lesions were discrete, rounded, slightly elevated, flat papules or wheals, somewhat shiny in some situations. There was no mucous membrane involvement.

DISCUSSION

DR. SCHAMBERG thought this might be a case of lichen planus. He would have sodium cacodylate administered as a therapeutic test.

DR. STRAUSS felt that the pigmentation might be the result of thyroid extract given this patient.

KAPOS'S SARCOMA. Presented by DR. SCHAMBERG.

A white man, aged 64, was the subject of this disease of three years' duration. Both legs were involved from several inches above the knee to the sole. The color of the affected parts was of a deep bluish red. There was considerable edema below the knees and the patient suffered pain, especially when walking. Improvement followed roentgen-ray therapy so that the characteristic appearance was gone, but there were still some distinct small bluish nodules on the sole of each foot. A number of small sessile tumors were present between the ankle and knee of each leg.

DISCUSSION

DR. HARTZELL agreed with the diagnosis but considered the use of the word sarcoma unfortunate in this disease, so unlike the surgical sarcoma. Dr. Schamberg suggested angiosarcoma as a preferable term on account of the vascular element.

MACULAR ATROPHY. Presented by DR. HARTZELL.

A middle-aged white woman had been under the speaker's observation for the past two weeks. She had an extraordinary condition which had existed for two years, resembling many of the cases reported as macular atrophy though it is not certain that all the cases so labeled are truly that disease; some are associated with scleroderma. The condition in this case may have been related to scleroderma. Numerous macules were located on the face, neck, shoulders, upper chest and back, varying in size from that of a pea to that of a postage stamp. Interspersed were as many pits formed by depressed atrophic areas of skin. The macules were waxy in appearance, the atrophic spots a dead white, giving the affected region a mottled look. It resembled numerous small scars. There was some itching, but it was not intense. On the back appeared slight scaling on the macules, which were barely elevated, infiltrated and firm.

DISCUSSION

DR. SCHAMBERG felt that this case was properly classified. The appearance of macular atrophy was produced during the transition from the indurated to the diffuse form of the disease.

PAPULONECROTIC TUBERCULID. Presented by DR. WARREN WALKER.

A white boy, aged 12, presented dystrophia unguium involving all nails of all extremities. Two brothers and a grandfather were similarly affected. Several small circumscribed crusted areas were present on the dorsum of each hand, and the palms showed horny papules with hard centers closely resembling papulonecrotic tuberculid. These had been present since the age of 2 years. Some were quite flat, and nearly all showed the hard central plug. One brother had had a similar eruption for some years, but the disease had cleared up in his case.

ECZEMA. Presented by DR. MAURICE BROWN.

A white girl, aged 8, showed a crusted eruption involving principally the neck and extremities. This condition appeared when the patient was 4 months old and had persisted obstinately ever since with the exception of short remissions following acute infections. There was much thickening of the integument in the affected areas with crusting and fissuring, chiefly on the extensor surfaces. The skin elsewhere was dry and harsh and resembled that of ichthyosis. The diagnosis was eczema with, most probably, an underlying ichthyosis. The case was exhibited mainly to show the inveterate character of the eczema, which had resisted many forms of treatment.

LICHEN PLANUS. Presented by DR. BROWN.

A comparatively noninflammatory eruption on the forearm, arm and neck was present in a white boy of 7 years. At the base of the neck were small annular lesions, and on the flexor surface of the forearm typical lichen papules were to be seen. There was some linear grouping. The eruption caused an itching sensation.

HETEROCHROMIA PILORUM. Presented by DR. CLARENCE K. DENGLE.

A white boy, 8 years old, showed an unusual condition which had been present since birth. Most of the hair of the scalp was of a chestnut color but from a small area of scalp on the vertex, irregular in outline but about the size of a quarter dollar, grew hair of a bluish-black hue. The appearance of the scalp in this region was normal; there was no nevus or a pathologic process discernible. The impression conveyed was that of a smear of ink on the surface of blond hair. Both parents had dark hair.

DISCUSSION

DRS. HARTZELL and SCHAMBERG did not recall a similar case.

EPITHELIOMA. Presented by DR. WARREN WALKER.

The age of this patient, 27, and the appearance of the lesion on his lip would at first glance have made the observer think of chancre which the history of four years' duration, gradual extension from a small beginning and absence of concomitant syphilitic signs, as quickly dispelled. He had served in the army while having the disease and had been under the observation of the presenter over two months. Adenopathy of the glands of the anterior chain was noted. The patient smoked considerably and had the habit of biting his lower lip, which possibly accounted for the somewhat atypical appearance and swelling.

PRURIGO NODULARIS (?). Presented by DR. STRICKLER.

Following an operation for hernia seven years ago, a man of 50 developed small nodules in his skin, causing intense itching, confined to the arms, legs and trunk. Macroscopically the disease closely resembled prurigo, although the course was quite unlike that condition. The Wassermann reaction was negative and examination of the blood shed no light on the condition. The tuberculin test was also negative. A biopsy was made.

NEVUS UNIUS LATERIS. Presented by DR. KNOWLES.

A white girl, aged 5, in good health in other respects, presented an eruption on the right lower leg, none of the growths being above the lower margin of the knee cap. The patches were brownish, slightly elevated, infiltrated and sharply margined. While irregular in outline, they were rather elongated in shape. The surface was slightly scaly. The condition had been present since infancy.

HERPES ZOSTER AND SYPHILIS. Presented by DR. BROWN.

On the left side of the chest of a white man, aged 48, were several areas of redness and pigmentation marked with numerous small pitted scars. These patches swept downward and outward from the spine in the regular zosteriform distribution, but were unusually large. There was present in the right axilla a small patch of a somewhat different character. The right buttock showed an ulcerating gumma, and the Wassermann reaction was weakly plus. All the eruptions have improved as the patient was on antisyphilitic treatment, and the scarring from the zoster has faded in color.

PITYRIASIS ROSEA. Presented by Dr. GREENBAUM.

A man of early middle age, apparently Jewish, exhibited on the trunk, upper arms and thighs a number of slightly scaly, rounded patches the size of half a dollar, pinkish to salmon in color and with slight infiltration. Interest lay in the fact that the rings seemed anesthetic to the pin test. The duration of the condition was only three weeks.

DISCUSSION

Dr. HARTZELL considered the case one of pityriasis rosea with hysterical anesthesia.

LYMPHANGIOMA. Presented by Dr. SCHAMBERG.

A white girl, aged 17, showed a rounded, elevated lesion on the buccal mucous membrane. It was first noticed during her first year. It was reddish, firm but compressible and sharply circumscribed.

CASES FOR DIAGNOSIS. Presented by Dr. SCHAMBERG.

A generalized eruption was present in a mulatto woman aged 29. Only the head and lower part of the legs escaped. For sixteen years she had been affected with a severely itching, papular eruption. No vesicles were seen or known to have been present, but most of the primary lesions were destroyed by scratching. Many excoriations and some pigmentation existed on the trunk. The causation was indefinite and diagnosis was withheld.

A former farm-hand, a negro 48 years of age, complained of intense itching for the past eighteen months. His arms and body presented numerous infiltrated lesions which resembled prurigo nodules in size and feeling, but a great part of the intervening skin was thickened and horny. The papules likewise had a horny covering. The lymph nodes in the axillae, neck and groins were quite prominent, some being the size of an egg. There was a leukocytosis of 60,000 with eosinophilia, but no lymphocytosis.

ECZEMA FROM TYPHOID INOCULATION. Presented by Dr. GREENBAUM.

A young man, a fireman, developed an eczema of the hands two years ago, the disease coming on three weeks after the completion of typhoid prophylaxis. Desensitization by small doses of typhoid vaccine caused the eruption to disappear, and it was later reproduced by a full dose. The second attack occurred four months ago, and has not responded to desensitization. There was an edematous condition out of proportion to the superficial character of the eruption. The hands were puffy and the fingers swollen.

CASE FOR DIAGNOSIS. Presented by Dr. GREENBAUM for Dr. SCHAMBERG.

A white woman, aged 55, presented a condition which was first noticed two years ago. The lesions were located on her lower legs and forearms. A bleb the size of a half dollar was present on one lower leg and a smaller one on her left forearm. Numerous circumscribed atrophic areas were noted roughly corresponding in size to the bases of the bullae. The latter showed no tendency to spontaneous rupture and some seemed to dry up unbroken. They pursued a slow course, leaving a distinct atrophy at their site. There was no pain, no mucous membrane involvement and no internal medication which might have been responsible for the outbreak. Biopsy was not permitted.

PHILADELPHIA DERMATOLOGICAL SOCIETY

*Regular Monthly Meeting, Dec. 13, 1920*MILTON B. HARTZELL, M.D., *presiding*

LYMPHANGIOMA. Presented by Dr. HARTZELL.

A white boy, 9 years of age, born in Hungary, was brought to the Skin Dispensary of the University of Pennsylvania Hospital several weeks ago with an eruption in the left lumbo-abdominal region. There was a history of a unilateral, grouped vesicular outbreak preceded by pain and, as an appearance of crusts grouped in zosteriform fashion was present, it was thought to be a case of shingles. A mild ointment to soften the crusts was prescribed, and the surface cleared. At a subsequent visit a new crop of blisters had developed, antedated by pain in that region, according to the mother. An old transverse linear scar, about 5 inches long, formed the equator of the largest patch of vesicles, and beneath this region was felt a deep-seated doughy mass the size of two palms. The scar was caused by an operation performed in Hungary. The vesicles occurred in two or three other patches in the same region. Most of them were coalescing and were not easily ruptured. A few were the color of normal skin, but the greater number were pinkish, darkening to purple. The superficial condition was a lymphangiectasis, the deep one a lymphangioma. The recent history was at first misleading.

DISCUSSION

DR. SCHAMBERG agreed with the diagnosis. Lymphangiomas of the skin were often associated with fibrous tissue in the deeper parts and were mixed growths, fibrolymphangiomas.

DR. HARTZELL once had a patient with a similar condition, who was ill-advised to open some of the vesicles, thus starting a flow of lymph which persisted for several days, soaking dressings and clothes.

A CASE FOR DIAGNOSIS. Presented by Dr. HARTZELL.

A white woman, aged 50, exhibited an eruption of about twenty years' duration. It began as areas of scaliness scattered over the body, more or less generally, in the situations in which infiltrated red patches later developed. The latter were large and frequently palm-sized, some even larger and none smaller than the outline of an egg. Probably thirty were present. They were not sharply margined, were considerably scaly and but slightly itchy. The scalp was clear, as were the hands and feet. Several patches had undergone spontaneous involution, atrophy and wrinkling of the skin resulting. The intermammary cleft and the mesial aspects of both breasts showed a sharply margined, raised plaque of a brighter red color. This was probably a keloid, as the patient gave a history of a burn there when a child. A biopsy was made, but the report has not yet reached the presenter. The Wassermann reaction was weakly positive. The patient received some arsphenamin therapy, and stated that the scaliness had improved since then. No tumors existed.

DISCUSSION

DR. SCHAMBERG considered this case rather remarkable. There was enough infiltration present to rate it as a neoplasm. He thought it might be an anomalous type of parapsoriasis.

DR. KNOWLES said that mycosis fungoides was suggested when he first saw the case.

DR. HARTZELL said that the spontaneous involution and atrophic scarring certainly suggested granuloma fungoides. There was marked infiltration.

ATROPHODERMA PEMPHIGOIDES. Presented by DR. GREENBAUM (DR. SCHAMBERG).

The case shown at the November meeting, that of a Jewish woman of 55, with lesions, apparently blebs, followed by atrophy, was shown again. New bullae had formed on the lower legs and left forearm. They were brownish in color and flaccid, though tense when first noted. They were deep-seated and had a thick roof, as evidenced by venules present in the latter. As they progressed the fluid was absorbed and the fibrous tissue of the floor of the bleb atrophied, so that when this had occurred the examining finger felt, as it were, a buttonhole in the skin. It was not absolutely certain that the lesions contained fluid, but the patient said that she pricked one and obtained a bloody liquid. She would not permit one to be opened by a physician. The name atrophoderma pemphigoides appeared to be appropriate.

DISCUSSION

DR. HARTZELL remarked on the similarity of the atrophy to that seen in some cases of leprosy—not intimating that this case had any other suggestion of that disease.

DR. SCHAMBERG said he had never seen this picture before in all its aspects. The blebs when seen early were tense, but later became wrinkled, as though the contents were absorbed.

DR. GREENBAUM spoke of the new bleb on the forearm. It had appeared since the last meeting and had been noted throughout its course.

EPITHELIOMAS. Presented by DR. PFAHLER.

A white patient, aged 57, began to receive treatment for an epithelioma of the glans penis the last of August, 1920. It had been noted three months earlier. He was treated with radium; 100 mg. were applied over the growth and 50 mg. in the urethra beneath it. The time of exposure in each of the three positions was two hours. The neoplasm disappeared without loss of tissue. In two months there was no sign of return. The roentgen ray was used over the groins for the control of metastases.

The second patient was a man of about the same age, who began to receive treatment Sept. 23, 1920, for epithelioma of the end of the tongue. There was distinct glandular enlargement. Radium was used on the surface and by needles in the substance of the growth. The roentgen ray was used externally, and later the radium applications were renewed. The growth and the glandular enlargements have both disappeared.

A CASE FOR DIAGNOSIS. Presented by DR. A. STRAUSS.

A white man, aged 40, exhibited a generalized eruption. It seemed to begin, according to the history given by the patient, as an urticarial rash, which in the course of five months appeared as rather small, flat shiny papules. They were quite discrete, well scattered and showed abraded tops from scratching.

Excoriations abounded among the lesions. There was an indistinct tendency to dermatographism. The lesions were most pronounced on the trunk, arms and thighs. Itching was intense.

DERMATITIS HERPETIFORMIS. Presented by DR. WARREN WALKER.

The eruption on the patient, a white man of 56, began as a bullous erythema multiforme about six months ago. The backs of the hands, neck and face were affected and the outbreak seemed to be a typical one. Instead of clearing completely, however, an eruption of a different type began on the trunk, arms and legs as a sudden widespread efflorescence of papules and vesicles, changing the appearance to that of dermatitis herpetiformis. The lesions were thickly set and often pigmented. They were transient and came out in successive crops. The case was a hospital case, and the patient resisted treatment for some time. The itching was severe and many excoriations and abraded papules, mainly on the back, were present. The grouping was not especially characteristic. Under treatment with cacodylate of soda given hypodermically there had recently been some improvement.

MYCOSIS FUNGOIDES. Presented by DR. STRICKLER.

A white man, aged 42, had a typical premycotic case of this disease. Scaly red, infiltrated plaques, varying in size from that of a silver dollar to that of two palms, were numerous on nearly all parts. There was some itching. None of the areas had disappeared recently. Arsenicals were being used, but the disease was practically stationary.

PARAPSORIASIS. Presented by DR. HARTZELL.

The speaker had recently seen three cases which bore a distinct resemblance to one another. They were rather hard to classify. All bore some resemblance to syphilis, and the patients had been treated for that disease, though they had negative Wassermann reactions. The patient exhibited, a white man of about 30 years, had had the disease for four years. The Wassermann reaction had been negative on three different occasions. A series of three arsphenamin injections had produced no improvement. The condition began as red maculopapules, which later developed scales. There was no itching. Cervical adenopathy was present.

DISCUSSION

DR. KLAUDER remarked that the case appeared to be one of parapsoriasis.

DR. SCHAMBERG said it bore resemblance to pityriasis lichenoides.

DR. HARTZELL added that a biopsy had been of no assistance in determining the type. There was no eruption in the palms of this patient, but there had been in the palms of others of the series. The eruption was macular at first. While he called it parapsoriasis, he deplored the name as it was used to cover a number of unrelated conditions.

ARSPHENAMIN DERMATITIS. Presented by DRs. SCHAMBERG and KLAUDER.

A young, white woman, after receiving two injections of arsphenamin less than a week apart, suddenly developed an erythematous eruption which came out a week after the last injection. It was more or less generalized but was

most severe on the neck and chest. The duration was three days. At first it was morbilliform in appearance. An injection had extravasated, produced cellulitis and induration, and it was felt that she had been sensitized thereby.

CHICAGO DERMATOLOGICAL SOCIETY

Regular Meeting, Nov. 17, 1920

CLARENCE A. BAER, M.D., *Presiding*

LICHEN PLANUS ATROPHICUS ET SCLEROSUS. Presented by DR. FISCHKIN.

The patient was a woman, aged 26 years, with white, atrophic spots, intermingled with flat papules surrounded by a vermilion border on the neck, chest and shoulders, which had been present for three months.

DISCUSSION

DR. LIEBERTHAL thought the case was a fine example of lichen planus atrophicus.

MOELLER'S GLOSSITIS OR GEOGRAPHIC TONGUE. Presented by DR. STILLIANS.

A Jewess, aged 23 years, married, had had pulmonary tuberculosis in 1918 and 1919, but left the sanatorium in good condition in 1919. In January, 1920, the sides of her tongue became sore and rough, and ring-shaped lines appeared, which changed position from day to day. The tongue gradually grew more painful, and the condition interfered greatly with eating, being irritated especially by acid foods, hot, spicy or hard foods. Salt produced much irritation.

The sides of the tongue were rough with deep fissures, in some of which could be seen short segments of the yellowish lines seen on the surface. These lines were about 2 mm. in width, dull yellowish-white, slightly elevated, disposed in short segments, and were more or less curved. At the sides and lateral part of the dorsum were smooth areas from which the filiform papillae had disappeared while the circumvallate papillae remained. Some of the smooth areas were crossed by the yellowish lines. General examination had revealed a hyperthyroidism and intestinal intoxication, and the patient has improved on a strict diet. She had received one short period of radium therapy which she thought relieved the pain a great deal.

DISCUSSION

DR. SENEAR was inclined to disagree with the diagnosis of Moeller's glossitis. The appearance of the margins of the tongue was not in keeping with Moeller's glossitis, as there were patches with whitish margins which he felt were typical of lingua geographica. He had recently seen the last case of Moeller's glossitis reported by the late Dr. Harris and had found the patient suffering intense discomfort, especially when eating. He had recommended the retirement of the man from railway service, although the clinical appearance of the condition was so insignificant that he felt that medical officials of the company might be skeptical.

DR. STILLIANS said the patient complained of intense burning and pain, and at the time of first coming under observation, there were distinct areas of denudation on the tongue. The patient had improved greatly under radium therapy and dietary management.

DR. ORMSBY recalled the fact that he had demonstrated a case of geographic tongue before the Society last year, and at that time had reported a series of six cases relieved by radium therapy. In the present case, in addition to the fissures of the margins, there were definite areas on the surface of the tongue.

DERMATITIS HERPETIFORMIS. Presented by DR. STILLIANS.

An Irishman, a tower switchman, 28 years of age, had had the disease for the past eight years, and had taken Fowler's solution until he had arsenical keratoses on the palms and soles. Autoserum, roentgen rays, ultraviolet light (Kromayer lamp), green soap and sulphur rubs and various drugs and foreign proteins had been tried in an effort to remove the lesions. There had been temporary improvement from the autoserum and the rubs, but none from the other methods. Of late, tincture of cannabis indica in 20 minim doses four times a day had given relief. For the past two months he had had a severe scleritis of the left eye, which Dr. Brown Pusey considered a part of the dermatitis herpetiformis. It was slowly improving under mild treatment with atropin.

DISCUSSION

DR. LIEBERTHAL was convinced that the use of the ultraviolet ray over all involved areas was of great value in the management of this itching dermatosis.

DR. SENEAR said that a recent article in one of the French journals stated that roentgen therapy gave excellent results in the treatment of these cases, but that in the discussion following one of the men stated that he had obtained even better results with the use of the violet ray.

DR. STILLIANS stated that he had tried the ultraviolet ray, and either his technic was at fault or the method was of value only in certain cases. He had given enough light at each treatment to produce a moderate erythema.

A CASE FOR DIAGNOSIS. Presented by DR. STILLIANS.

An American, aged 38 years, a kitchen steward, two years before had noticed a red spot the size of a pinhead on the tip of the nose. No subjective symptoms were present, but the spot had slowly enlarged. Just under the tip of the nose was a tumor 0.3 by 0.5 cm., oval, with a rounded top, covered with telangiectases, soft and appearing pale yellow under the diascope.

DISCUSSION

DR. BAER thought the case was one of epithelioma, and that it was probably cystic.

DR. OLIVER had seen a similar lesion on the neck, which had yielded readily to radium therapy.

DR. LIEBERTHAL could not accept the diagnosis of epithelioma. There was definite scaling on an angiomatous basis, and he was of the opinion that the case was one of angiokeratoma.

INFECTED NEVUS. Presented by DR. OLIVER.

A man, aged 24 years, had had a large portwine nevus over the buttocks and down the posterior surface of the thighs. Following a rather strenuous horseback ride when a small boy, he had developed numerous ulcerating nodules about the saddle region. The nodules had continued until the present time. In spite of the presence of these lesions, he had been accepted for military service.

SCLERODERMA. Presented by DR. ORMSBY and DR. MITCHELL.

The case of a girl, aged 16 years, was first demonstrated before the Chicago Dermatological Society, Oct. 15, 1909. The condition had been present since birth. At that time the skin of the forearms, legs and hands was described as resembling cigaret paper. When shown in 1909, the process had extended to the middle of the upper arm and nearly to the crotch on the legs. Since that time there had been practically no extension.

The patient was a dwarf in stature and the arms were relatively much shorter than normal, the tips of the fingers reaching only to the trochanter. The menstrual function began at 14 and apparently was normal. There was no impairment of intelligence. The skin of the arms was thickened in localized patches, whereas in others it was definitely atrophic. The pigmentation persisted. The skin of the legs was still somewhat thickened and in places scaled. The linear verrucous lesions on the outer surface of the right leg persisted.

The patient had been given thyroid from August, 1915, until June, 1918, at which time pituitary substance was substituted.

DISCUSSION

DR. EISENSTAEDT thought the case was one of acrodermatitis atrophicans, and that it was worthy of much study from the standpoint of general medicine, especially of endocrin functioning. He thought there should be a determination of the basal metabolism. The conformation of the bones was decidedly abnormal, and he believed there was probably thyroid and ovarian insufficiency.

DR. LIEBERTHAL believed Dr. Eisenstaedt's suggestion was good. There was marked infiltration of the legs, but the arms were distinctly atrophic, and he was convinced that the case was one of scleroderma. In questioning the mother, he had found that the condition had begun shortly after birth. In such cases there was usually complete healing, as was shown in the hitherto reported cases.

DR. SENEAR stated that he was in New York at the time when Dr. Wise was working on his series of cases of acrodermatitis atrophicans and had the opportunity to see one of his cases. He did not think that it corresponded with the condition in the case shown, which he considered an atypical scleroderma.

DR. ORMSBY considered the case interesting because of the therapy employed. There had been a gradual progression of the disorder for nine years, despite the fact that the patient had received thyroid gland therapy almost continuously. If there had been any thyroid insufficiency, that should have been compensated for by the treatment given. The child was mentally and sexually well developed, as was shown by the fact that the menstrual periods began before she was 14, and, as far as he knew, there had been no disturbance of

that function. Hence, there probably was little, if any, ovarian insufficiency.

In regard to acrodermatitis atrophicans, that disorder always begins with infiltration and is followed by atrophy. In this case infiltration had not preceded the development of the present condition. He agreed to the suggestion that there was probably some endocrin disturbance, but felt that the thyroid and ovarian secretions were not at fault. He believed the condition was scleroderma.

PSORIASIS OF PALMS. Presented by DR. ZEISLER.

The patient was a man, aged 24 years, with a well defined red patch occupying the greater part of the left palm, with a small area in the right palm. The lesions were dry and covered with grayish-white scales, and had been present for six years.

DISCUSSION

DR. LIEBERTHAL thought it was a case of palmar psoriasis, but believed it was quite unusual for the lesions to be limited to the palms for six years.

DR. ORMSBY said he had reported a similar case a number of years ago and had seen another on the day preceding the meeting. The first patient had developed generalized psoriasis some years later. Therefore, he was convinced that there could be no doubt that psoriasis was limited to the palms for a considerable period of time.

DR. EISENSTAEDT concurred in the diagnosis, and stated that he had had a case similar to the one mentioned by Dr. Ormsby. At the time of the first visit, the patient had had three small lesions on the penis and had later developed characteristic lesions in the scalp. He felt that the duration of the lesions for six years with no other manifestations of the disease was quite remarkable, but in his opinion there could be no doubt about the diagnosis.

DR. ZEISLER said that Dr. Pardee had reminded him of a statement that had often been made by Dr. Zeisler, Sr., to the effect that psoriasis of the palms occurs only once in a million cases.

DERMATITIS HERPETIFORMIS. Presented by DR. ZEISLER.

The patient was a man, aged 27 years, a machinist, whose eruption had been present for eighteen months. It began on the body and spread to the chest and limbs, never entirely disappearing. The lesions were papular and urticarial, with pigmentation from former lesions. Itching was severe the greater part of the time. The patient was in good health, had been married six years and had no children. Venereal infection was denied.

DISCUSSION

DR. LIEBERTHAL believed the diagnosis of dermatitis herpetiformis was correct.

TUBERCULOSIS. Presented by DR. E. M. MILLER (by invitation).

A man, aged 32 years, presented an enlargement of the left side of the upper lip. The disorder had started four months before as a small ulcerating papule on the mucous surface opposite the left lower canine tooth. Beneath this ulcer swelling occurred and increased rapidly with moderate pain. After

several weeks a biopsy was performed, and a histologic diagnosis of carcinoma was made from the original growth. At a later date a submaxillary gland was removed, which showed typical tuberculosis. (These slides were exhibited.)

At the time of presentation there was a distinct indurated swelling involving the left side of the upper lip, which was neither painful nor tender. There was no change in the color of the skin over the area. Comparatively recently, radium and roentgen therapy had been employed, but as yet they had had no effect on the growth.

DISCUSSION

DR. EISENSTAEDT wanted to know whether radiotherapy had reduced the swelling to any appreciable degree. Microscopically the lesion on the lip was not characteristic of epithelioma. He thought that tuberculosis of the glands could be reduced effectively, though, of course, not rapidly, by properly filtered massive dosage. The rays should be hard and passed through thick filters.

DR. LIEBERTHAL said that judging by the clinical appearance of the case and study of the sections from the glands, he believed the case to be one of tuberculosis, although there was a suggestion of malignancy in the section taken from the lip.

DR. SENEAR had examined the sections, and he was not convinced that the lesion on the lip was malignant. It reminded him somewhat of the lesion shown by Dr. Zeisler last year, which was later demonstrated to be tuberculosis.

DR. ROSE (Presbyterian Hospital) stated that she had treated the lesion with 82 kilovolts through 4 mm. of aluminum for 48 milliamperes-minutes at a time, cross-firing in four directions, and using 9 inch focal distance. Six treatments had been given.

DR. BAER thought the lesion of the lip was malignant and that the glandular condition was tuberculosis. He did not agree with Dr. Eisenstaedt about the rapidity of results with radiotherapy in tuberculosis. In his experience, tuberculous glands had yielded slowly and persistence was necessary to obtain any appreciable results.

DR. MILLER (E. M.) was convinced that the giant cells in the glands closely resembled those occurring in tuberculosis. He welcomed any suggestions in regard to management of the case.

DR. ORMSBY thought the condition would prove to be tuberculosis, although it was not typical. As to response to radiotherapy, it had been his experience that improvement had been very slow. About 50 per cent. of the patients improved, whereas in the other 50 per cent. there was no improvement at all. He would not have expected the condition in the present case to improve in this short time with the amount of treatment given. Malignancy, in his experience, responded rapidly, but this was not the case with tuberculous processes. If the upper lip were malignant, it should have improved markedly.

NOTE.—On Dec. 9, 1920, the disorder had improved without further treatment.

VERRUCA PLANA OF THE TONGUE. Presented by DR. STILLIANS.

An American, an instructor in a university, aged 32 years, had a wart on the dorsum of the left middle finger which had been present for eighteen months and one that had been present for about the same time on the tongue.

On the dorsum of the tongue, near the tip, was a flat, round, pale papule, about 0.3 cm. in diameter, slightly elevated, and on the dorsum of the middle finger of the left hand was a large, flat wart.

A CASE FOR DIAGNOSIS. Presented by DR. MACKEY.

The patient was a man, aged 20 years, an office clerk. The disorder had first appeared on the left hand about ten months before. When 14 years of age he had had a chapped, scaly condition of the lips, and a reddened, scaly condition between the toes, and slight similar attacks had occurred since that time.

At the time of presentation there was some dandruff over the scalp with a crust the size of a coin in the occipital region; the margins of the eyelids were mildly inflamed and scaly; an erythematous band or halo, $\frac{1}{2}$ inch wide, was present around the vermilion border of the lips, which was slightly scaly. The patient asserted that on account of the irritation and dryness, he frequently moistened these surfaces with the lips. The palmar surfaces of the hands and fingers and the plantar surfaces of the feet and toes, extending over the dorsum of the fingers and toes, were covered with flakelike, desquamative scales, and these surfaces, being denuded, were brightly erythematous. Previous to the application of an ointment prescribed by another physician, these parts were covered with massed grayish-yellow crusts. The patches were sharply defined, had always remained dry and no itching was complained of. There was slight scaliness and erythema in the inguinoscrotal fold. The Wassermann reaction was said to be negative.

DISCUSSION

DR. ORMSBY thought the margins of the lesions in the palms looked like the advancing border of the lesions of dermatitis repens.

DR. LIEBERTHAL said that the lesions on the lips and scrotum were, in his opinion, those of seborrheic dermatitis.

DR. OLIVER thought Dr. Ormsby would recall the case of a patient with similar lesions on the palms shown by the late Dr. Schaffner. The lesions failed to respond to all methods of treatment.

DR. ZEISLER suggested the diagnosis of psoriasis.

DR. SENEAR said that he had seen many borderline cases which offered a great deal of difficulty in the diagnosis between psoriasis and seborrheic dermatitis. In this case he first thought of psoriasis, but the lesions on the lips and in the scalp strongly suggested those of seborrheic dermatitis.

DR. BAER believed the case to be one of psoriasis.

BROMID ERUPTION. Presented by DR. OLIVER.

A man, aged 24 years, had received moderately large doses of bromid in the treatment of epilepsy. On withdrawal of the bromid, the lesions had healed, but had left numerous disfiguring scars over the back, arms and legs.

Book Review

PHYSIOLOGY AND PATHOLOGY OF THE CEREBROSPINAL FLUID.

WILLIAM BOYD. The Macmillan Company, 1920.

The preface of this volume expresses its scope well. "The object of this book is to present some of the fascinating physiological problems connected with the cerebrospinal fluid, and to show how they are related to the pathological problems which more directly concern the clinician. Not until the method of production and absorption of the fluid is completely understood can there be any hope of solving the age long problem of the treatment of hydrocephalus; not until the details of the circulation of the fluid have been mastered, can intraspinal injections of drugs and sera be expected to fulfill the hopes of the therapist.

"Any means which will facilitate the difficult diagnoses of the central nervous system is of value, and the cerebrospinal fluid, which bathes its deepest recesses and washes the very nerve cells and fibers themselves, is in truth a mirror which reflects every change taking place in that system."

The book is divided into two parts. The first, or general section, deals with the anatomy, the origin, circulation and function of the fluid, and its physical, chemical and cellular composition. In addition, there are chapters on lumbar puncture, the Wassermann reaction, and the colloidal gold reaction of Lange. The section comprises about eighty-six pages.

Part 2 deals with specific problems. The chapter of especial interest is that devoted to syphilis of the central nervous system. The newer work on this phase of syphilitic infection is well reviewed. The whole tendency has been to place ever earlier the period at which the nervous system may become infected, until we have reached the stage in which cases are being reported in which the cerebrospinal fluid shows changes said to be characteristic at the same time as the appearance of the primary sore. It is certain that in the general systemic infection which marks the commencement of the secondary stage the nervous system not only is not exempt, but is in reality one of the parts of the body most frequently involved. In the present state of our knowledge we cannot say which of these cases will speedily clear up and which will develop into incurable parenchymatous syphilis, nor do we know the factors on which this depends.

By the term cerebrospinal syphilis, which, although admittedly unsatisfactory in the light of our present knowledge, has passed into such general usage that it is difficult to dispense with it, Boyd includes all forms of what Mott has termed interstitial syphilis, that is to say, cases in which the parenchymatous elements of the nervous system are not primarily involved. The three principal types are the gumma, syphilitic endarteritis and syphilitic meningitis, or meningo-encephalitis. Tabes dorsalis, general paresis and juvenile general paresis are the other nervous system conditions considered under the head of the nervous system. In the condition of juvenile general paresis, the cerebrospinal fluid shows the same pathologic changes as in the adult form of the disease. The four reactions and the Lange test are all positive.

The various reactions in those forms of syphilis which affect the nervous system are suggested in the following table. The plus sign indicates that a positive result is obtained in nearly every case. The Wassermann reaction in the fluid is reckoned on the assumption that 0.2 c.c. were used.

	Secondary Syphilis	Cerebrospinal Syphilis	Tabes Dorsalis	General Paresis
Wassermann test of the blood.....	+	+	70%	+
Wassermann test of the spinal fluid	—	30%	60%	+
Pleocytosis.....	50%	+	+	+
Globulin.....	—	+	+	+
Lange (paretic curve).....	—	—	—	+

A subdivision of the chapter on therapeutics is devoted to the intraspinal treatment of neurosyphilis. The method and technic of arsphenamin administration as advocated by Swift-Ellis and the later modifications of the idea are given in about eight well written pages.

The book contains 176 pages. It is faultlessly printed and contains five black and white illustrations and six colored plates. A desirable feature is the list of references given at the close of each chapter.

The book is to be recommended for those desiring a short, yet modern and inclusive discussion of the physiology and pathology of the cerebrospinal fluid.

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XX.—THE APPLICATION OF CUTANEOUS SENSITIZATION TO DISEASES OF THE SKIN *

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ST. LOUIS

Theories of cutaneous sensitization and their application, as advanced by Chandler Walker in the determination of a state of allergy to certain proteins in relation to asthma, have proved of great clinical interest, and when desensitization could be carried out, of inestimable therapeutic value. It is obvious that this method, if applicable to diseases of the skin, would be of assistance in the determination of possible etiologic factors in a large group of them. It is not our object at present to consider at length the various theories of anaphylaxis or sensitization and their application in the cutaneous tests. To enter this maze of literature would, in this instance, occupy unnecessary time and require needless effort. We shall, therefore, limit our remarks to the purely practical aspect of the subject.

To Chandler Walker we are indebted for a method of grouping the various proteins in such a way as to render the determination of sensitization practicable. To determine for ourselves the practical value of this method in the study of various skin diseases, we selected for investigation a large number of diseases, including those that we thought might possibly have some relationship to so-called protein sensitization. The following diseases were studied in this way in an effort to determine their relative cutaneous reaction to various proteins: acne, urticaria, erythema multiforme, lichen urticatus, pompholyx, purpura hemorrhagica, pemphigus, trade dermatitis, dermatitis vegetans and the large eczema group. The method used in carrying out this investigation differed only in minor variations from that employed by others. The protein products were obtained from the Arlington Chemical Company of Yonkers, N. Y., and were made by them under the

* Read at the Forty-Fourth Annual Meeting of the American Dermatological Association, Asheville, N. C., April 22-24, 1920.

* Studies, observations and reports from the dermatological departments of the Barnard Free Skin and Cancer Hospital and the Washington University School of Medicine, St. Louis, Mo., U. S. A., service of Drs. M. F. Engman and William H. Mook.

directions of Walker. They proved to be reliable products. Lately, we have been using those of Squibb, and of Parke, Davis and Company, with seemingly accurate results.

Patients on whom the tests were made were drawn from the dispensary of Washington University, Barnes Hospital, the Barnard Free Skin and Cancer Hospital and private practice. Confirmatory diagnoses of two or more clinicians were always made before classifying the disease. A detailed history was taken in every case, in an attempt to establish an etiologic clue of a positive sensitization to aid in the first tests. To do this, inquiry was always made as to the duration of the disease and its relation to climatic, occupational, seasonal or other conditions that might possibly have some bearing on the case. If there seemed to be any relation to food, the patient could often assist materially in narrowing the list of proteins in the first test by giving a definite history of exacerbation following the ingestion of a certain food or foods. If there was no seeming associations obtainable in the history, these food proteins were then tested: wheat, milk, egg, beef, pork, and in addition, such others as the case might suggest.

Occupation was always carefully inquired into to determine any possible associations, or to ascertain whether similar conditions were found among fellow employees. Inquiries were also made as to freedom from, or recurrence of, the condition in relation to absence from, or return to, occupation. Climatic influence was always regarded of importance in its relationship to the aggravation or relief of the condition. Attempt was also made to fix a relationship between seasonal foods or pollens. Other associated relationships which it was found necessary to consider constantly were: time (day or night), companionship, focal infections, worry, neurasthenia and unusual traumas. If the patient seemed to obtain relief from any measures employed as suggested by himself, they were often of material assistance in throwing some light on possible etiologic factors, whether due to sensitization, autointoxication or external irritation of some offending substance.

The tests were uniformly made on the inner surface of the forearm. Only exceptionally was it necessary to resort to other parts of the body for this purpose. For each test, a small incision, about $\frac{1}{8}$ inch long, was made through the epidermis, with a very sharp von Pirquet scarifier, having a semicircular tipped blade. This form of instrument has no corners but rather a circular cutting edge which, with slight pressure and a rocking motion, produces the least trauma in making the incision. Every precaution should be exerted to avoid trauma in making the incision, as the dermographic or urticarial tendency of some patients is so marked as to interfere with proper development of positive reactions.

These little incisions were placed about 1 inch apart. Each incision was then moistened with a drop of $\frac{1}{10}$ normal sodium hydroxid solution to which there was at once added a minute quantity of the protein preparation to be tested. One-half hour's time was always allowed for the full development of the reaction. Often, however, positive reactions were manifested within a few minutes. Cleaning the surface of the arm in preparing the field for the test was avoided or done an hour or so before the tests were made—a precaution which should be observed, as alcohol or other antiseptic agents influence the reaction. Alcohol particularly tends to reduce the surrounding erythematous areola in positive reactions, in some instances resulting merely in very small wheals or none at all. In very sensitive skins, the friction is sufficient to produce a condition of dermatographia, which always interferes with the proper development of the reaction or the interpretation of results. The cleaning of a site was, however, at times necessary, to remove chemical substances that might have come in contact with the skin. This was brought to our attention by observing that, in certain instances in which local therapeutic application had been made to the skin before the tests were made, the proteins failed to go into solution, or were promptly precipitated on coming in contact with the sodium hydroxid solution.

When thirty minutes had elapsed after the incisions were made and the protein applied, the skin over the area was wiped with dry or moistened cotton, and developments were awaited. The results were read according to Walker's method, that is, in comparison with control tests, grading the positive reactions as +, ++, +++ and ++++, and were checked by reaction development measuring $\frac{1}{4}$, $\frac{1}{2}$, $\frac{3}{4}$ and 1 cm. This graduation, however, will not be used in this report as no constant relationship was found to exist between the intensity of the positive reactions and the clinical manifestations of the disease. Moreover, some very positive reactions consist only of erythematous areolas without the development of wheals.

When this study was first undertaken, it was impossible to secure bacterial protein preparations and only a limited number of pollen solutions were available. The tests herein considered were uniformly made for egg-white, egg-yolk, beef, wheat, potato, milk, bean, horse-dander, with the addition of such proteins as the history of an individual case might suggest, or with less common foodstuffs. Bacterial and pollen tests were not made as a routine, but only in those instances in which the history of the case suggested them. On account of the limited variety of bacterial proteins, tests were made only with those of the *Staphylococcus albus*, *aureus* and *citreus*. The pollen tests were limited to ragweed, cornflower, goldenrod, timothy and sunflower.

In keeping with the observations of other investigators, subsequent tests frequently yielded positive reactions that had previously been negative.

Tests made at various times differed in the degree of their reaction, which suggests the possibility that the condition of sensitization in individuals may run in the form of cycles in which the line curves in a definite period above or below the normal. This phenomenon is well brought out and discussed by Schloss¹ under the general title of allergy. When a positive reaction occurs with a protein that exists in a number of foodstuffs in a certain group, it will be seen that a person reacting to this protein will probably react in a milder degree to several other proteins of foods belonging to this group; for instance, if sensitization to beef exists, all other meats may also produce a similar but milder reaction. This rule holds good with the proteins of grains, especially wheat, in which there may be a sensitization giving a reaction to the proteins of several other grains.² A similar phenomenon occurs with the epidermal protein and the casein group. Confusion frequently arises from this fact and renders the interpretation more difficult, especially in guiding one in the application of diet.

Like all other investigators of this subject, we could not obtain absolute control of our patients and their diet except in a few instances. Unless control is thus obtained, the study is seriously handicapped. It is obvious to every one that it is impossible to control a patient's diet in the large majority of instances, unless he is confined in a hospital provided with a proper diet kitchen, and the directed diet accurately given. Most of our patients were from dispensaries or from private practice, where the absolute control of the ingested foods was impossible. Patients are proverbially thoughtless and sometimes ignorant of the constituents of the foods which they eat. For instance, in a state of wheat sensitization, they would thoughtlessly eat spaghetti or allow flour to be added to gravies or soups, thus invalidating the wheat-free diet. Unless proper inquiry into every article of the diet list was made by the physician in attendance, well controlled results could not be obtained. In the case of infants, the elimination of one or more proteins from the diet was easier, since the patient's own choice of food was not a factor, and with the cooperation of an intelligent mother in the matter of such simple diet, absolute control could in most instances be obtained.

Improvement under dietetic control, followed by exacerbation on return to the diet containing the suspected proteins, will always indicate,

1. Schloss, O. M.: Allergy in Infants and Children, *Am. J. Dis. Child.* **19**: 433 (June) 1920.

2. The work of Osborne and Wells might be commented on at this point. Theirs were the first studies on protein relationships.

with a fair degree of certainty, the tolerance of the patient, which may vary from absolute intolerance to the allowance of a considerable quantity of the offending food.

TESTS AND RESULTS

1. *Acne*.—Eighteen cases of acne vulgaris were used for this test without any specific result. Sixteen of them were negative; two suggested slight positive reactions to wheat and fish, which shows a negation in summing up the results obtained in this disease.

2. *Dermatitis Herpetiformis*.—This disease is undoubtedly due to some form of toxemia. One of us (Engman) has demonstrated several times the close relationship that seems to exist between this affection and intestinal putrefaction. Focal infections in the teeth or at other sites may be etiologic factors. Drugs have been known to precipitate dermatitis herpetiformis, as pointed out by Hartzell and Engman. For instance, in the administration, under special conditions, of potassium iodid to susceptible persons, a definite eruption of dermatitis herpetiformis characteristic in its clinical and histologic phases may result. If dermatitis herpetiformis is caused in certain susceptible persons by the administration of drugs, it shows definitely a drug genesis, using the word in the broadest sense. Therefore, other toxemias or toxic bodies circulating in the blood stream may precipitate an attack. In this study, eleven cases typical of the disease were investigated, in which only one gave slight reaction to horse dander, a protein which obviously produces its greatest damage through external or local influence, causing dermatitis.

3. *Urticaria*.—The etiologic factors in producing this large group of diseases may be divided into two classes, both of which are blood-borne: (1) by the distribution of emboli or micro-organisms; (2) by the contamination of the blood stream by some chemical body admitted into the body through foodstuffs, the action of micro-organisms, intermediary metabolism, or other sources or foci from which toxic bodies may emanate. In the latter subdivisions, we must include parenteral introduction of protein, as in serum disease.

It is in this large group of diseases, obviously of toxic origin, that we should obtain very interesting and instructive results from cutaneous sensitization. We must admit that the offending toxin, whatever it may be, produces the eruption by a specific action on the cutaneous capillaries, and not on the vasomotor centers or indirectly through the vasomotor nerves. All histologic pictures of this group show definite symptoms of inflammation, as pointed out by von Dühring, Philipson and Gilchrist.

Nineteen patients were investigated, fifteen of whom reacted in some manner to this test: five to egg-white, one to salmon, six to wheat, two to cheese and one to beans. All of these were cases of urticaria of the usual type, and very satisfactory therapeutic results were obtained whenever the diet could be controlled absolutely. Two cases were particularly interesting. One was an iron-worker who had had chronic urticaria for many years. The least trauma would cause enormous wheals to appear, and the resulting factitious urticaria would so handicap the patient that he had to discontinue his work. He showed a marked cutaneous sensitization to wheat, and as we were able to control his diet, wonderfully satisfactory results were obtained. At various times he tested his own susceptibility by eating wheat, with the inevitable recurrence of the traumatic urticaria. Gradual return permitted the inclusion of whole slices of wheat bread. He could also eat toast and cereals, when they were thoroughly toasted.

Another patient, a woman, aged 45, in whom chronic urticaria had existed for many years in the ordinary traumatic variety, was found to be very sensitive to casein. She had been put on various diets and had been treated by some of our leading gastro-enterologists, with no relief from the chronic urticaria. As it happened, a cutaneous test had not been made before. Through this test, it was demonstrated that the patient was sensitive to casein, cheese and milk, and when these articles were eliminated from the diet, excellent results followed. Boiling the milk and skimming off the coagulated casein did not seem to act favorably in her case.

In this urticarial group were several patients with the ordinary type of sensitization to egg-white. Of all varieties of proteins, egg-white and wheat seem to be the ones to which the largest number of these patients react. All of these improved under proper restriction of diet. In some, a return to the offending food produced exacerbation.

4. *Erythema Multiforme*.—Of the pure Hebra type of erythema multiforme, six patients were tested, all with negative results. Several of these were tested many times.

5. *Lichen Urticatus*.—Four patients were tested, two of them several times, with negative results.

6. *Pompholyx*.—Four patients were tested, with one positive result. This patient shows pork sensitization up to the present time, and obtains prompt relief by elimination of pork from the diet.

7. *Pemphigus*.—Two patients were tested, with negative results.

8. *Purpura Hemorrhagica*.—Three patients were tested, with negative results.

9. *Trade Dermatitis*.—We have herein included those cases of dermatitis due to occupation, such as that found in cement workers, chem-

ical workers, dentists, etc. There were nine patients tested, all of whom were negative to protein sensitization.

10. *Dermatitis Vegetans*.—One patient was tested, with negative results.

11. *Eczema*.—We have now come to the group of diseases that are supremely interesting from the standpoint of cutaneous sensitization, namely, that large group of diseases known by the generic term eczema. It is not necessary here to enter into a discussion of the nomenclature or the pathology of the members of this group. First, for the sake of convenience, and to avoid confusion, we will convey the clinical picture according to the present nomenclature, using terms familiar to all in the designation of types.

(a) Erythematous Eczema: Seven patients were observed who were of extreme interest in relation to cutaneous sensitization in its broadest aspect. Six of them were free from any detectable protein sensitization, yet their skins were peculiarly irritable and reacted to the slightest traumas, such as wind, dust, sunlight or any other slight influence.³

One was sensitive to oak pollen and had suffered from erythematous eczema from this source for nine years. It began in April, lasted through the spring, and was accompanied by typical attacks of hay-fever. Later, under the care of Chandler Walker, the patient obtained relief through desensitization.

(b) Chronic Eczema of the Generalized Type: There were twenty-one patients, eight of whom showed cutaneous sensitization: one to *Staphylococcus aureus*, four to wheat, one to egg, one to wool and two to horse dander.

(c) Localized Eczema: These eczemas were localized on the flexor sides of the elbows or knees, etc. Two patients were negative, and one was positive to wheat.

(d) Acute Eczema: It was found on examination of the patients with acute eczema that none was sensitive to any of the proteins that we had on hand, which proved that most of the very acute forms of eczema were due to purely external chemical causes, such as hair dyes, fur dyes, cleaning fluids, cosmetic, medicines, linaments, or other sources of acute dermatitis, including various poisonous plants. One peculiar case of erythematous dermatitis was that of a man who suffered strange attacks of a recurrent dermatitis of the face. On investigation, his condition proved the result of a bleach that his wife used for her hair, which affected his skin as he rested his cheek against her hair or against the pillow that she had used.

3. Two of these patients were probably photosensitive, or were the hemato-porphyrin types of Hausman.

REPORT OF CASES

CASE 1.—M. S., a girl, aged 16, had had relapsing attacks of eczema for some years due to *Staphylococcus aureus*. She was easily desensitized with great success by *Staphylococcus aureus* vaccine in increasing doses.

CASE 2.—A girl, aged 15, had had eczema since babyhood. Her case belonged, no doubt, to that class which Czerny has called exudative diathesis, eczematous attacks recurring frequently throughout life. She was only partially benefited and then when in the confines of the hospital. Had it been possible to obtain the full cooperation and confidence of the patient, we are certain, judging from our short experience with the case, that the results would have been brilliant.

CASE 3 (common).—A man, aged 54, had had a chronic dermatitis or eczema on the face, hands, neck and ears, almost continuously for four or five years. The eruption at times disappeared, and then returned within a few hours, characterized by a tingling sensation, accompanied by erythema and edema of the area affected, always followed by itching, exudation and dermatitis. He had no knowledge whatever of food sensitization, and his reaction to wheat, at the time of observation, was weak. As he was an intelligent man, he cooperated and excluded wheat from his diet, which was practicable only when he was not away from home on his customary trips. Under these conditions, he was completely relieved of all symptoms.

CASE 4.—J. H. D., a woman, aged 56 years, had a dermatitis of the face and forearms, almost of the vesicular type, which had troubled her for years, disappearing and reappearing at times. She had strong sensitization to wheat, but under proper diet, she rapidly improved.

CASE 5.—C. D. D., a woman, aged 30 years, had a very severe erythematous eczema of the face, forearms, neck and scalp. The attacks came before we began this investigation. The patient lost all the hair of the scalp, and recovered very slowly. She did not, however, remain perfectly well, until we discovered her sensitization and then placed her on a diet. She stated on April 12 of this year that when she ate bread or wheat in any form, the skin of her face became erythematous and swollen, accompanied by intolerable itching. Rye bread then replaced wheat bread in her diet, and her physician ordered a new cereal, in which, however, wheat was detected by the violent cutaneous reaction within two hours after eating.

CASE 6.—All the symptoms of an eczema in a physician, who had a sensitization to wool protein, were alleviated when he discarded woolen underwear.

CASE 7.—A huckster, aged 35 years, was sensitive to horse dander, and because of his constant exposure to his horses, he suffered with continuous dermatitis. Owing to his occupation, we were unable to obtain satisfactory results, but we are now attempting desensitization.

CASE 8.—W. L., an oil speculator, aged 33 years, who had had erythematous eczema for fifteen years, was very sensitive to horse dander. His condition had the same history as all the other cases of this type, becoming better at times and remaining so for some months, then reappearing suddenly over night. When his attention was called to horse dander, the reason for his attacks became clear to him, and he remembered that his first attack occurred at the time he had a pet dog of which he was fond and accustomed to handle a great deal. He also recalled subsequent attacks on visits to horse sales or stock-yards. He is now being desensitized. (It is curious to note how animal dander

from almost any animal may cause an outbreak of symptoms in those sensitized to any of them.) Through the patient's own observation, he relieved his itching at night by removing feather pillows and woolen blankets.

CASE 9.—G. R., a man, aged 50, had complained of eczema every summer for the last five years. In winter, his skin was clear, and the patient thought it was entirely normal. At the time of the first visit, his entire face, neck, ears, arms and hands were covered with an exudative crusted eczema. His lip was drawn and covered with crusts. At first, he gave a very doubtful reaction to tomato pollen. Further inquiry elicited the fact that the present skin condition superseded the setting out of young tomato plants. Tests were repeated in about six days, using juice from tomato vines. These resulted in a very positive erythematous reaction that developed slowly, however, and was developed only after twenty-four hours. This reaction was not an urticarial lesion but a distinct red pin-point vesicular eruption about 1 cm. in diameter.

(*e*) Infantile Eczema: This is the *bête noire* of all dermatologists. It was with great interest that we approached this part of our study and the results have been both satisfactory and unsatisfactory: satisfactory as far as the tests gave a clue to the etiology of the condition, but most unsatisfactory as far as control and outcome of treatment were concerned. The type of disease, so well described by Czerny as exudative diathesis, stands out as typical for most of those infants who have eczema. The disease usually begins on the face as an erythematous blush and extends to the extensor surfaces of the extremities. If the baby be not carefully watched and be allowed to scratch or rub the parts, the entire body not infrequently becomes involved. Four cases of infantile eczema which localized persistently in portions of the body other than the face or extremities, were excluded from this study, because irritation of various kinds in these areas obscured the picture.

Of the exudative type (thirty-six in number), 78 per cent. responded positively to some protein sensitization: nine to egg-white (only), two to egg-white and milk (cows), six to milk (mother's only) five to milk (cow's only) and six to wheat (only).

Unfortunately, the majority occurred in dispensary practice, and therefore were uncontrollable as to diet. But in those cases in which we were able to encourage or receive cooperation on the part of the mother, brilliant results were obtained.

REPORT OF CASES OF INFANTILE ECZEMA

CASE 1.—S. B., aged 4 months, had the usual dermatitis. The cutaneous test showed a reaction to mother's milk. When put on proper feeding, the patient immediately responded, the itching subsided, and the eruption disappeared. After a period of some weeks, there was a relapse, and after another test, the baby was found very sensitive to beef protein. The diagnostic accuracy of this test was substantiated when the mother confessed to having fed the child beef tea. The baby at this time showed sensitization to both milk and beef. On discontinuing the beef tea, the skin condition immediately cleared.

CASE 2.—M. B., aged 5½ months, reacted positively to cow's milk. It was suggested that goat's milk be tried, and the eruption disappeared coincidentally. Because of the previous condition of the child, which had caused the mother considerable worry, she was advised to place it in a hospital for a while. While in the hospital, the child was again fed cow's milk, and a severe relapse of the cutaneous condition followed, and when it was once more put on goat's milk, this condition subsided. It is interesting to note that when the mother was in the hospital, an eminent pediatrician attempted to feed the child on a proper modification of cow's milk, but without success, the intense pruritus and eczema relapsing.

CASE 3.—F. J. B., a boy, aged 2½ years, had a typical case of exudative diathesis. The cutaneous test showed a doubtful egg-white reaction. As the child had been eating eggs freely, it was put on an egg-free diet with rapid and brilliant results. Within a few days the face was almost free from the eruption.

CASE 4.—J. K., a girl, 3 years old, presented a severe case, which had begun shortly after birth. The skin of the face and extremities was thickened, yellow, pasty and showed patches of eczema. The glands at the angle of the jaw and in the neck were enlarged. The child was a mouth breather, a condition which would probably continue for years unless the cause was discovered and eliminated. The child proved distinctly reactive to wheat. Fortunately, in this instance, we had the cooperation of a very intelligent mother. The baby appeared for treatment on April 2, 1919, and was completely well on May 23, 1919. She was presented at the joint meeting of the Chicago and St. Louis Dermatological Societies in October, 1919, and not the slightest symptoms of her former disease were to be found. The enlarged glands had disappeared, her skin was soft, pink, smooth, healthy and beautiful. Strange to say, even the mouth breathing had disappeared. The mother stated that if the child was given a cracker, for instance, for breakfast, in the afternoon she would begin to scratch and rub her skin because of erythematous welts that appeared on the cheeks and extremities.

We might say in passing, that pruritus of the face and extremities seems to be the first symptom produced by the disturbing protein. Thus, traumatism is induced at the sites of the itching by rubbing and scratching, which establishes a dermatitis that is usually increased by local agents, such as staphylococcic infections, lotions and salve. In some instances, distinct erythematous blotches, or wheallike lesions, seem to precede or cause the intense itching. Some of these children madly toss themselves from side to side in paroxysms of itching. When the itching is produced by some sensitizing protein, the pruritus is in many instances wonderfully and quickly relieved by the removal of that protein from the diet.

The four cases just described have been quoted for illustration. It is needless to continue with other such cases, as the literature now presents many of them. Our studies lead us to believe that of the 78 per cent. in this group, showing protein sensitization, all could have been brought to a satisfactory therapeutic conclusion, had we had absolute control of the diets. This being the fact, the future treatment

of infantile eczema depends: first, on the accuracy with which the cutaneous sensitization test is performed and interpreted; second, on the accuracy in following the therapeutic path which that interpretation directs; third, on repeating tests at intervals to determine the exact status of the case in relation to protein sensitization.

SUMMARY AND CONCLUSIONS

1. In urticaria, 79 per cent. showed a positive sensitization; in infantile eczema, 78 per cent. and in chronic generalized eczema, 38 per cent.

The percentage is almost negligible in such diseases as dermatitis herpetiformis, erythema multiforme, lichen urticatus, pemphigus and purpura hemorrhagica, although one might say that a sufficient number of cases of the latter diseases had not been investigated.

2. The necessity of a thorough investigation of cutaneous sensitization is shown in the first four conditions.⁴

3. This study presents an interesting comparison with that of Baker,⁵ who, under the title of "Incidence of Protein Sensitization in Normal Children," showed "that the incidence of positive protein sensitization in normal children is negligible." This emphasizes the significance of the high percentage we have obtained in eczematous children, and corresponds with the statistics of Blackfan, who showed a protein sensitization as high as ours in infantile eczema. Blackfan goes further and states that children without eczema rarely give a positive test.

4. From the excellent results obtained in so many cases in this study, we are forced to the conclusion that the cutaneous sensitization tests by the dermal method is of inestimable value as a diagnostic and therapeutic measure in the study and care of urticaria, eczema and several other diseases of the skin.

5. It is obviously necessary that a study of a case, from the standpoint of protein sensitization, must include those proteins with which the patient may come in contact in his daily life, an extremely laborious study and one that requires time and patience.

4. We should like to call attention to the fact that we were not able to carry out extensive studies with bacterial and pollen proteins in our early cases, though now complete lists of products are available. Also, that no special proteins were prepared for study of special cases, which (obviously) should be done, if full value is to be derived from this diagnostic method.

5. Baker, H. M.: Incidence of Protein Sensitization in Normal Child, *Am. J. Dis. Child.* **19**:114 (Feb.) 1920.

6. From the therapeutic standpoint, the physician is greatly handicapped by not having complete control of the patient's diet, which, however, has nothing to do with the method from its purely diagnostic application. Our efforts have given us, we might say, in every instance in which we could exercise control, the most excellent results, and, when desensitization was possible, the diet in many instances could be resumed.

7. We have not at present sufficient experience with desensitization to speak dogmatically of its merits, yet we believe from this experience that it has as great a future in the cutaneous field as in that of asthma and other affections of the air passages.

OCCUPATIONAL DERMATITIS IN DENTISTS: SUSCEPTIBILITY TO PROCAIN

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Occupational dermatitis in dentists has usually been laid at the door of some one of their antiseptics, or soaps, or in an indefinite way referred to some one of the many substances which they handle. Frequently the patient, a dentist, is informed that sooner or later experience will show the particular agent which is causing his condition. An examination of the textbooks and literature does not reveal, except in one instance, any evidence of a dermatitis associated with local anesthetics. Mook,¹ in a recent paper, has reported the case of a dentist with susceptibility to apothecin, and in reporting this case states that procain gave much the same reaction as apothecin when skin tests were applied. The dermatitis in this case, however, cleared up when the use of apothecin was stopped. The attention of the profession has apparently not been called to the fact that procain may be an etiologic factor in some of these cases. It is the factor, without doubt, in the three cases which I have to report. These dentists, who have practiced for a number of years, who have used procain over a period of months, have had an irritated condition of the hands, which appears to be due to their individual susceptibility to procain. This dermatitis did not develop immediately when they began to use the drug, but appeared after it had been employed by them as a local anesthetic over a period of months. This fact may be interpreted as an indication that the condition was fundamentally an acquired susceptibility rather than a real idiosyncrasy—a susceptibility of unexplained or idiopathic origin.

The fact that procain can be added to the list of substances which are the cause of cutaneous manifestations in susceptible persons warrants a few statements about the drug. Procain was introduced by Einhorn, and was clinically tested and exhaustively written about by Braun in 1905. It was most widely used among dentists, and also for local anesthesia in surgery. It was introduced into this country about 1912, and is apparently the local anesthetic most widely used among

1. Mook, W. H.: Skin Reactions to Apothecin and Quinin in Susceptible Persons, *Arch. Dermat. & Syph.* 1:651 (June) 1920.

dentists, and also for local anesthesia in surgery. It has numerous advantages over cocain. It is six or seven times less toxic; it will keep for a long time without deterioration; its action is increased and prolonged by combining it with epinephrin; it does not cause the least irritation on injection; it is soluble in its own weight of water. Le Brocq makes the statement that it is equal to cocain in its anesthetic properties. Gwathmey is responsible for the statement that after absorption the general effect on the system is scarcely perceptible, neither the circulation nor the respiratory system being affected. There is no mydriasis, no disturbance of accommodation, and no increase of intra-ocular pressure. It is neutral in reaction, and its solutions are precipitated by alkaloids and alkaline carbonates, although it is not affected by sodium bicarbonate. It is apparently a much more satisfactory drug to use than cocain.

The three dentists whom I have seen recently because of a dermatitis of the hands have been in practice for many years, and have been using procain for some months. The eruption on their hands has appeared since they began to use this drug. Since discontinuing its use, or wearing gloves, the irritation has disappeared and their hands have become normal. Furthermore, the evidence of skin tests has been in agreement with the clinical evidence.

REPORT OF CASES

CASE 1.—Dr. A. has practiced dentistry for twenty-three years. He has used procain occasionally for one year, and exclusively for two years.

History.—In May, 1920, itching began between the fourth and fifth fingers on the right hand, which gradually extended to other fingers; the fingers became red and fissured, and there was some oozing. Itching had been most intense at times.

Examination.—Examination in July showed considerable scaling, with fissuring of both palms and about the fingers. There were circinate, almost serpiginous areas with numerous scales, considerable redness, and a suggestion of vesiculation. There was much redness between several of the fingers, and there was a deep fissure between the fourth and fifth fingers on the right hand, and a fairly deep fissure at the base of the fourth finger on the palmar surface, in addition to other less active fissures. The condition of the right hand was much worse than that of the left hand, especially on the ulnar side. The palms, at this visit, gave the impression of an epidermophyton infection. Examination of the scales was negative, but the clinical appearance warranted the use of half-strength Whitfield's ointment. Examination of the scales at the end of twenty-four hours in potassium hydrate solution revealed no mycelia, but there were numerous highly refractile bodies suggesting spores.

Course and Treatment.—In two weeks there was distinct improvement, both objectively and subjectively. The itching became less, and the fissures healed, leaving only slightly scaly and red areas between the fingers and the sites of former open fissures. The skin became more normal. An area of vesiculation and redness appeared about the nose, right cheek and lip, which at this time

was thought to be caused by the irritation which resulted from the transference of some of Whitfield's ointment to the face.

At the end of two weeks more, new areas had appeared on the hands, areas which were more vesicular and grouped, with recurrence of fissures and burning and itching, especially on the middle and forefingers of the left hand. At this time inquiry was made into the chemicals which the patient was using, particularly the ones which he had begun to use most recently. At this time procain was suggested as a possible cause, and he was advised to use rubber gloves during his work, and to alternate between a weak Whitfield's and Lassar's paste. His hands became better, the fissures closed, and there remained numerous areas of dry, scaly skin, with few fissures which were dry. There was no redness and no vesicles, and the itching had gradually disappeared.

Skin Tests.—Six weeks after his first visit skin tests were made on his forearm with the solution of procain which he customarily used. It contained procain, 2 per cent., in Ringer's solution, with a slight amount of chloretone as preservative. The tests were performed, using this solution, with and without suprarenal extract, and using an old solution made up ten days or two weeks previously. In twenty-four hours there was intense redness and itching at the points of inoculation with all procain solutions. The old solution gave the greatest reaction, showing a rather intense red area, 1 cm. in diameter, elevated, with severe itching. Controls were negative.

At this time he went on his vacation and on his return in three weeks reported that his hands were normal while away, even though subjected to fairly hard usage. They were just as well as ever on his return to work. He has continued using procain solution, but has worn gloves when using the solution. In spite of this fact, he has one or two small fissures on his hands, and there is occasionally more or less itching. He has had slight irritation and redness about the right corner of his mouth, and recalls squirting some of the procain solution on his face several days before. The previous irritation on his face probably resulted from a similar accident. On his forearm there are still redness and slight thickening of the skin at the site of previous inoculations the point of application of the old procain solution showing as a distinctly purplish area about 1 cm. in diameter. Itching and redness persisted, the patient states, for two weeks after inoculation.

Another series of tests was made in confirmation of the first series, using the same solution as previously, using suprarenal tablets alone, and using cocain solution. At the same time a similar series was performed on my own forearm, the results of which were all negative. The results were absolutely confirmatory, similar reactions being produced as at the previous tests. An additional fact of interest at this time was that after the solutions had been applied about fifteen minutes a sudden motion of the patient's forearm spilled the solutions to the inner side of the forearm. Evident traces of the solution were found for many days over the areas which had been covered in the spilling. Severe itching and redness and distinct streaks were produced where the procain solution had traveled. The use of procain had been given up and the hands were practically clear save for slight scaliness in patches, and one or two dry fissures. No new lesions and no new vesicles had appeared.

A third series of tests was made on the forearm, using six solutions: (1) Ringer's solution; (2) procain E (Metz), 2 per cent., with epinephrin; (3) procain F (Metz), 2 per cent., with epinephrin; (4) procain T (Hoechst), with epinephrin (different make); (5) cocain, 1 per cent., with epinephrin, and (6) sterile water. Within twenty-four hours there were redness and eleva-

tion about 2, 3 and 4, greatest about 3. There was the same intense itching, with redness extending for 5 mm. about the region of inoculation, with slight elevation, the whole process, and the redness, lasting for nearly two weeks.

CASE 2.—Dr. B. has practiced dentistry for thirteen years and had used procain two years before symptoms appeared.

History.—In November, 1919, he began to have redness of the skin about the nails, with fissuring of the nails and adjacent skin and itching, especially of the left hand. Later a similar condition appeared between the fingers and on the palms. The left hand had always been most severely affected. The process had always been more localized about the fingers and nails than elsewhere. There had been itching and oozing, with much serum exuding at times. The nails had been rough, cracked, corrugated, with some suppuration, both at the base of the nails and below the nails at the finger tips. He had been using Whitfield's ointment part of the time, and had been careful in regard to the use of soap. For one period of three or four weeks, and for several shorter periods, he had been unable to work because of his hands.

Six days before his visit to my office in October, 1920, he was told by Dr. A. (referred to in the preceding case report), of the possibility that procain might be the causal agent. At that time he had fissures beneath the nails at the tips of the first and third fingers on the left hand, and about these two nails especially, together with severe general itching and burning of the hands. At that time the right hand had much the same feeling with areas of redness and oozing on the approximating surfaces of the third and fourth fingers. He gave up the use of procain on this date, and he stated that the itching and burning had become gradually less and that the hands had become drier and less red.

Examination.—On the day of the examination, six days after stopping the use of procain, the left hand showed considerable fissuring about the nails, with redness and exfoliation below the tips. The skin at the bases was thickened and rough as in a chronic paronychia. The first three fingers were dry, rough and scaly. The last two fingers were nearly normal. On the right hand the nails were much better than on the left, but were rough and more or less corrugated and dark colored. Between the third and fourth fingers there was an area of redness on the fourth finger, with slight vesiculation on the side toward the third finger. There was also a small, red, crusted area on the dorsum of the fourth finger just behind the nail where the ball of the third finger rested while working. His position at work, holding an instrument, showed closer approximation and pressure on the spots mentioned. On the right forearm, near the wrist, on the palmar side, was a small papule where procain had been dropped about five days previously. The patient also gave a story of accidentally squirting some of the solution from the needle on his face, near the nose, some time ago, followed in from twenty-four to forty-eight hours by intense itching and redness.

Course of Disease.—Five days after his first visit, his hands showed much improvement. The left hand showed practically all normal skin. There were no signs of the previous condition about the middle finger nail. The right hand was all clear except on the thumb side of the fourth finger where there were a few small papules, dull red in color, which were not itching. The area on the dorsum of the fourth finger had disappeared entirely. The patient stated that he must have washed his hands forty times the day before as a matter of experiment, but his hands seemed no worse. He was still continuing to use cocain for extraction.

Skin Tests.—At this time skin tests were performed with (1) sterile water; (2) procain, 2 per cent.; (3) apothecin, 2 per cent.; (4) cocain, 2 per cent.; (5) a solution containing procain and epinephrin in Ringer's solution (solution four or five months old); (6) procain, 0.5 per cent. These solutions were applied and allowed to remain for thirty minutes. In twenty minutes a definite wheal, irregularly 5 mm. in diameter, appeared about number 2. About number 6 was a similar blanched area, but only 2 mm. in diameter. About number 4 was a slightly red area with slight elevation. The other areas simply showed a redness at the point of rotation of the dental burr. In twenty-four hours there was a distinct red papule about number 2 and number 6, with considerable itching. In forty-eight hours there was at number 2 a red papule, 5 or 6 mm. in diameter. The redness was rather intense, and there had been much itching about this particular inoculation. There was a slight redness and elevation for an area 3 mm. in diameter about number 5. About number 6 there was a slightly larger area of redness with a little more elevation. All of these had itched to some extent but not as much as number 2. The patient discontinued the use of procain and his hands have remained normal.

CASE 3.—Dr. C. has practiced dentistry for seventeen years and had used procain from two to three months before symptoms appeared.

History.—In August, 1919, Dr. C. began to have itching and burning of the hands, with considerable redness and the formation of blisters on the backs of the hands and between the fingers. At this time he had to give up work for three weeks on account of his hands. He had had urticaria occasionally but that is the only previous skin trouble which he had had. He began the use of "Novol," a procain preparation in Ringer's solution, about two months previously, in May or June, 1919. He dated the disturbance approximately to the time when he began to boil frequently this anesthetic solution for use. He believed that his hands became affected from the steam.

When he returned to work his hands were scaly, without any itching or redness. Within five days recurrence occurred, and he was away from his office for another period of three weeks. This time when he returned to his office his hands were in much better condition and practically normal. Three days after his return to work his hands became affected again, and at this time his face was much swollen and red, with considerable crusting. It was necessary for him to give up work for a period of three or four weeks. During the period when the disease was at its height the nails were discolored, brownish, cracked, and became separated from the bed, and later came out altogether. His hands were very greatly swollen, so that it was impossible to approximate the tips of the fingers. The area of involvement never extended above the edge of the coat sleeves and was only slight on the palms. The condition of both hands was about the same.

In the latter part of October he started to use rubber gloves all the time in his work and remained practically free from any skin disturbance of his hands. Since March, 1920, he has been wearing gloves in his practice only while using procain, and his hands have remained clear.

About three weeks before coming to my office he had not used his gloves for one day because his hands had been well so long. On this day he used procain on five or six patients, and two days later the second and third fingers of his left hand were much fissured, red, and oozing. He has returned to the use of gloves during the actual injection of procain, but he removes the gloves after injecting the anesthetic and putting away his instruments.

At the present time the first two fingers of the left hand are the only ones which show any variation from normal. Near the tips are red, slightly fissured

scaly areas which burn and itch slightly. The rest of the hand is normal. During the extraction of teeth the first two fingers of the left hand are naturally within the mouth of the patient, while the right hand grasps the forceps. These two fingers are the ones which are involved, and it is fair to suppose that the condition on the two fingers of the left hand may be due to the procain oozing from the gums. He has never had procain injected for any purpose.

Skin Tests.—Skin tests were performed on the inner side of the left forearm with (1) sterile water; (2) a proprietary brand of procain; (3) procain (Metz), 2 per cent.; (4) procain, 1 per cent.; (5) cocain, 2 per cent, and (6) sterile water. He reported in twenty-four hours on the skin tests, stating that number 3 showed slight redness. In forty-eight hours examination revealed (1) no reaction; (2) an area of slight redness, about 5 mm. in diameter, very slightly elevated; (3) a red area, 6 to 7 mm. in diameter, redness most intense of all, with extension of redness in one direction for 1 cm.; slightly more elevation than in 2; (4) an area about 5 mm. in diameter, paler than 3, with extension in one direction for about 1 cm. The patient stated that redness and itching appeared on the day of examination; that he noticed nothing the day previous; (5) no reaction; (6) no reaction. The redness and slight itching persisted for ten days or two weeks.

SKIN TESTS

The skin tests in these cases were performed on the flexor surface of the forearm, the site of inoculation being produced by the twirling of a dental burr rather than by the use of a sharp-edged instrument. Sterile water was used as a control, and the various constituents of the procain solution and tablets were used in order to avoid the possibility of any interaction, and in order to test each substance separately. The reactions produced were observed for thirty minutes, after twenty-four hours, and again forty-eight hours after inoculation. A description of the results of these examinations has been given to aid in the interpretation.

The evidence offered by skin tests is debatable ground. In these three cases the evidence of these tests checks up with the clinical findings and is corroborated by the results of treatment. Further investigations are under way to find the number of persons sensitive to these various local anesthetics, and a report will be rendered at some later date. It is expecting too much to hope that the results will check as closely in all cases, and I feel that the final test, as Rackemann² says, is the agreement between the skin tests and the patient's history before making definite conclusions from the evidence of the skin tests.

SPECIFICITY OF REACTION

There are certain points in these cases which will bear additional emphasis. In all three cases an eruption appeared on the face, in

2. Rackemann, F. M.: The Clinical Study of One Hundred and Fifty Cases of Bronchial Asthma, *Arch. Int. Med.* **22**:517 (Oct.) 1918.

all probability associated with the accidental application of procain. This fact, with the evidence of the skin tests, indicates the specificity of the reaction to this particular drug and that it is a systemic condition, not merely a localized disturbance. In one case there is the possibility of a concomitant infection with a fungus. In this relation it is possible to suppose that the moist, soggy condition of the skin produced by the dermatitis would act as an excellent medium for the growth of these organisms which may be almost normal inhabitants of the skin. In only one case was there evidence of immediate allergic reaction, as evidenced by the appearance of wheals at the sites of inoculation; but all three cases showed evidences of specific reaction by papules and redness at the points of inoculation forty-eight hours afterward.

Here are three persons apparently susceptible to a drug which they have handled extensively, who have shown signs of a dermatitis on areas which this drug has reached, who have reacted to skin tests specifically for this particular drug, and whose condition has cleared up on refraining from the use of this particular agent. Several other cases have come to my attention, though not seen by me personally, in which dentists with an irritated condition of the hands while using procain, have experienced much improvement in their condition after using rubber gloves constantly while handling such solutions. It would seem then that sufficient evidence is presented to affirm that a susceptibility to procain has been the cause of dermatitis in this group. Moreover, the lapse of time from the beginning of the use of the drug to the onset of the irritation suggests that the susceptibility is acquired rather than hereditary.

ANAPHYLAXIS OR ALLERGY

The fact of this susceptibility brings up for consideration the phenomena of anaphylaxis or allergy. It is an open question whether these persons have become sensitized by the constant handling of procain and whether this dermatitis is an allergic reaction. An attempt was made to ascertain whether it was possible that these persons had become sensitized by the previous use of procain internally, that is, at previous extractions of teeth or previous operations. No history of subcutaneous use of procain was obtained. Highman and Michael,³ in a recent paper, state that nothing is known of sensitization through normal integument, but that it is possible that the skin at these sites always presents microscopic injuries. In support of this they cite the case of an actor who developed angioneurotic edema following the application of grease paints, stating that this case may be a possible

3. Highman, W. J., and Michael, J. C.: Protein Sensitization in Skin Diseases: Urticaria and Its Allies, *Arch. Dermat. & Syph.* **2**:544 (Nov.) 1920.

example of parenteral sensitization. They also cite cases of guinea-pigs sensitized by inhaling sprayed foreign serum, and also call attention to the fact that sensitization through injured integument is conceivable because of the fact that extremely small amounts of alien protein may sensitize.

Can this drug act as an alien protein? It is known that other substances than proteins are able to produce reactions similar to those above described. The eruptive phenomena occurring occasionally after the administration of arsphenamin have been sufficiently impressed on our minds. Auer⁴ states that the suggestion has been made that certain drug reactions may depend on the formation of compounds between the drug and the body proteins so that substances similar to foreign proteins are formed, and that this accounts for the resemblance to anaphylaxis which drug reactions may exhibit. This hypothesis, however, has not been established. In a summary of his experimental work along this line, he states that anaphylactic reaction may occur because the inflamed tissues are more active metabolically than normal tissues, and, therefore, the inflamed cells are affected by more antigen per unit of time than normal cells. Thus a lessened concentration of antigen for noninflamed sensitized cells may become effective when inflamed sensitized cells are concerned.

CHEMICAL EXPLANATION OF ANALOGOUS CONDITION

It is hardly possible at the present time to offer any explanation, even a partial one, on chemical grounds, but it is worth while to consider a somewhat analogous condition in rubber workers which has recently been described and explained on the basis of certain known chemical facts. The recent work of Shepard and Krall,⁵ while not explaining the underlying cause of susceptibility, still makes an ingenious explanation of the causes of dermatitis associated with certain rubber workers. Their explanation is based sufficiently on known facts to make it appear plausible, and further investigation of causes along similar lines is justified from the work which they have performed. They report that certain of the workers in a rubber factory, which uses hexamethylenamin as an accelerator in the vulcanizing process, developed a dermatitis on forearms, arms and face, and were found to have a susceptibility to hexamethylenamin. They offer an explanation of the inflammatory process based on the fact that hexamethylenamin

4. Auer, John: Local Auto-Inoculation of the Sensitized Organism with Foreign Protein as a Cause of Abnormal Reactions, *J. Exper. Med.* **32**:427 (Oct.) 1920.

5. Shepard, N. A., and Krall, S.: Poisons in the Rubber Industry, *The India Rubber World* **61**:75 (Nov. 1) 1919.

is known to break down in the presence of acid and produce formaldehyd. The sweat is acid. The eruption is worse in hot weather. Formaldehyd alone does not produce a similar eruption. Formic acid does. They offer the explanation that possibly formaldehyd on the skin, in the hair follicles or glands, may be oxidized to formic acid, thus producing an irritation which is found in these workers. They offer as a solution to this condition the use of an alkaline solution. This treatment not only relieves the condition, but prevents its appearance, even in sensitized persons, when their hands and arms are immersed in the solution and allowed to dry before going to work. As I have said, no explanation is offered by these authors in regard to the underlying condition of susceptibility to hexamethylenamin, but the explanation of the cause of the dermatitis and its cure appears as a reasonable one.

POSSIBILITY OF GENERALIZED REACTIONS

It is interesting to conjecture as to the conditions which may be produced in persons susceptible to procain who subsequently receive injections for the extraction of teeth or for operative procedures. Do they have more local reaction, or do they have symptoms of a general nature? Dentists occasionally have patients who have become sick after a local anesthetic and may attribute that sickness to the excitement of the moment, to the actual extraction, possibly to sepsis afterward, or to the drug. There have not been, apparently, as many cases of illness produced after extraction of teeth since the use of procain, cocain apparently producing a greater effect on the person than the newer drugs. Three cases of death following procain have been found, one following extraction of teeth, and two following operative procedures on the antrum. All three of these were fairly sudden, and the case reports attribute these fatalities to the drug, although comment is made of the possibility that the operation and manipulation might have had some influence in the antrum cases.

The consideration of this subject of anaphylaxis in relation to dermatology by Highman and Michael, and Towle,⁶ in recent papers, gives an accurate estimate of the current opinion in regard to this subject. This subject is, as they say, wholly on a theoretical basis as yet, but the fact remains that more and more cases and more and more diseases are being considered as candidates for admission to this particular group of dermatoses, and further study and analysis of these and other conditions will undoubtedly contribute much toward their eventual explanation.

6. Towle, H. P.: Protein Sensitization in the Production of Skin Disease, *Arch. Dermat. & Syph.* 2:531 (Nov.) 1920.

CONCLUSIONS

1. In dermatitis of the hands in dentists procain must be considered as a possible causal factor.
2. The clinical observations, together with the confirmatory results from skin tests, indicate an individual susceptibility.
3. The possibility of sensitization by means of the skin in these cases is suggested.
4. The treatment is obvious—to prevent the drug from reaching the hands, either by supporting its use, or by wearing rubber gloves.

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A FIFTH CASE OF SCLERODERMA WITH ARSENIC IN THE URINE

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LOS ANGELES

Scleroderma as a manifestation of chronic arsenic poisoning was discussed in a recent issue of THE ARCHIVES OF DERMATOLOGY AND SYPHILOLOGY.¹ Four consecutive cases were cited, three of the diffuse variety and one of the localized type, in which arsenic was demonstrated in the urine. The following is the fifth case of the series.

REPORT OF A CASE

History.—F. W. (No. 299872), in the outpatient department of the Massachusetts General Hospital, was a housewife of Russian Jewish extraction who had lived in Boston the past thirteen years. She was 34 years old, and up to the time of her present illness, which began four years ago, she had always enjoyed good health. Her husband and four children were living and well; there had been no miscarriages. She had never engaged in any occupation outside of her own housework, and so far as she knew, had never used any arsenical preparations or been exposed to arsenic in any form; she denied the use of any medicines prior to her present illness. Although she denied the use of any medicine containing arsenic during her illness, and although the hospital records show that none was used, the possibility of having received it from an outside source cannot be positively ruled out.

Neuritic Manifestations.—Neuritic manifestations ushered in the present illness. Numbness and soreness of the fingers of the right hand, and a few weeks later of the left hand, were the first symptoms noted. Since then there had been soreness, aching and attacks of cyanosis of the hands, legs and feet, especially during cold weather. During the first year the hands, forearms, legs and feet frequently became swollen after activity but improved following rest. Excessive perspiration of the palms had been constant. During the past year she had had difficulty in sleeping.

Skin.—The patient believed that the brown pigmentation and patches of leukoderma had been present about a year. She did not recall definitely when the skin began to harden, but the process had been progressive.

General Condition.—There had been weakness and great loss of weight. Occasional lacrimation had occurred at night during the past year. There had been excessive flow of saliva at night during the past year, sufficient to wet the pillow. At intervals through the present illness, the tip of the tongue had been sore and burning, especially during cold weather. During the past four months she had had moderate sore throat. She had always had headaches which, during the present illness, had not been more severe than formerly.

Her appetite had been failing for the past two years. During the past eighteen months she had had attacks of pyrosis with eructations, relieved by

1. Ayres, Samuel, Jr.: Scleroderma as a Possible Manifestation of Chronic Arsenic Poisoning, Arch. Dermat. & Syph. 2:747 (Dec.) 1920.

soda and to some extent by taking food; there had been no vomiting. During the past three weeks the bowels had moved three or four times a day, and there had been abdominal cramps like "knives going around," often severe enough to cause the patient to go to bed. There have been no bloody or tarry stools.

There have been no symptoms referable to the cardiorespiratory or genito-urinary systems.

Examination.—The skin presented the most striking features. The areas of greatest involvement were the fingers, hands and forearms to just above the elbows. Here the skin was glossy, tightly drawn and infiltrated so that it could not be pinched up; the fingers were fixed in a claw-like flexion. These areas showed a brown pigmentation with a few patches of leukoderma. Both thighs were indurated but not pigmented. The lower two-thirds of the right leg showed pigmentation and sclero-edema; it pitted on pressure but the pitting remained a considerable length of time. The face was moderately involved; the pinnae of the ears were thickened, the nose was narrow and pointed with the skin drawn tight and the lips were narrow. Over the sternum the skin was infiltrated, and there were many telangiectases. The palms and soles were wet with perspiration, but there were no keratoses. Pubic hair was normal, but there was complete absence of axillary hair (the patient said she never had any). The scalp hair was of good quality but somewhat sparse; the eyelashes also were thin. The tongue was slightly coated in the center, but distinctly smooth and atrophic along the edges and tip. The tonsils were slightly large and red. The thyroid gland was not palpable; there were a few small palpable lymph glands in the neck. Knee jerks and plantar reflexes were absent; the pupils reacted to light. Sensation to pain and touch was normal. Both feet were flat. Aside from these findings, the physical examination was negative.

Laboratory Findings.—Routine blood and urine examinations were not made. The Wassermann reaction was negative. (Four years ago, at the beginning of her illness, the Wassermann reaction was reported positive at the Peter Bent Brigham Hospital, and she was given three intramuscular injections of mercury, but she failed to continue at the clinic; she received no arsenic there.) On August 19, a quart of urine was examined for arsenic by the Sanger method in the chemical laboratory of the hospital; no arsenic was found. On August 31, a second sample of urine and a specimen of hair were examined for arsenic, with negative results. The patient was then given a saturated solution of potassium iodid, ten drops three times a day; eighteen days later a third specimen of urine was tested, resulting in a definite positive qualitative test for arsenic. The presumption is that the potassium iodid combined with the arsenic, which was stored in the tissues, converting it into a soluble form which was easily eliminated, conforming to the reputation which potassium iodid enjoys in that respect. Putnam² has pointed out, however, that arsenic may be excreted only intermittently by the kidneys, and that even in acute fatal cases of arsenic poisoning the urine has been found free.

Recently Dr. Richard L. Sutton of Kansas City has added a sixth case to this series. His patient had the diffuse type of scleroderma and showed arsenic in the urine in an amount sufficient to quantitate. The test was made by the Kansas City Testing Laboratory. In neither of these two cases was the patient aware of the source of the arsenic.

2. Putnam, J. J.: Boston M. & S. J. **122**:421, 1890.

It is desirable to emphasize strongly a point which was made in the previous paper on this subject, namely, that no assertion is being made that an etiologic relationship between scleroderma and chronic arsenic poisoning has been established. The evidence is entirely circumstantial, and the series of cases is too small to justify definite conclusions. However, the facts seem sufficiently interesting to warrant presentation merely for what they are worth.

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THE VALUE OF IODIN IN THE TREATMENT OF LEPROSY

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HONOLULU, H. I.

Potassium iodid, which has been used more or less extensively in the treatment of leprosy, especially during the period between 1860 and 1890, has been considered by most leprologists as harmful rather than helpful in the treatment of the disease. Danielson, who, during the earlier part of this period, probably experimented on a larger scale than any other authority was, however, satisfied that this drug was of great value, especially in the tubercular form of the disease. Having used potassium iodid personally, in a limited way, I became, early in my experience in the treatment of lepers, quite convinced that the so-called harmful action was, in fact, a curative one. Instead of giving the ordinary dose of 10 to 15 grains daily, I gradually increased the dose to between 100 and 200 grains. In one special case I gave even more than that amount daily for many days. The patients suffered greatly at times, especially those with the nerve type of leprosy affecting the median and ulnar nerves. Excruciating neuralgic pains along the nerves caused many sleepless nights, but those who persevered in the treatment were greatly benefitted. Large nodules would break down into open ulcers, and would finally heal with but little scar tissue, leaving not a single leper organism in the healed tissue. Beginning contracture of the hands would be abated, and often the condition of the hands returned to normal, sensation being completely restored.

When I became medical superintendent of the Kalihi Receiving Hospital for Lepers, situated in the outskirts of Honolulu, in January, 1910, I began giving iodine in the form of sajodin, a 32 per cent. iodine powder, the dose being gradually increased to 20 grains three times a day. I also employed iodine in the form of Lugol's solution in increasing doses to 20 drops three times a day. Later I commenced to use iodalbin, an iodine preparation containing about 22 per cent. of iodine. Of the three iodine preparations, I prefer iodalbin. Neither sajodin nor iodalbin in 20 grain doses would cause iodism or discomfort to the patient, while Lugol's solution, if continued, was liable to cause considerable irritation of the stomach. Improvement at first was extremely slow, but after the first six months curative results in some cases were quite rapid.

IODINIZED AUTOGENOUS SERUM

In association with this intensive use of iodine internally, I have attempted to use an iodinized autogenous serum obtained in the follow-

ing way: Skin lesions containing large numbers of lepra bacilli are frozen with a carbon dioxid snow pencil to produce a large bulla. The fluid from these bullae is withdrawn under antiseptic precautions and reinjected into the patient. Different lesions are used from time to time, but any single lesion is employed until the bacilli can no longer be obtained from it. This process is repeated at seven to ten day intervals. The basis for this therapeutic method is the belief that iodine, which passes out through all the secretions, would be contained in the serum, thus forming an iodinated autogenous serum. Furthermore, the increased blood supply brought to the part treated with the snow pencil would produce a local phagocytosis, and would aid in bringing the iodine directly in contact with the diseased tissue.

I am firmly convinced that this method of using iodine has a curative action in the treatment of leprosy. In my Board of Health Report dated June 30, 1913, I made the following statement: "My former experience with iodine of potassium in leprosy, and the more recent use of sajodine, leads me to the belief that if it were possible to form an iodine compound after the manner of the arsenical compound known as '606' wherein the iodine could with safety be exhibited intravenously, a marked specific for leprosy would be had." Janin, in 1913, reinjected serum from bullae with good results but did not use the snow pencil to make the bullae, or give iodine internally at the same time. In 1916, Hollman and Currie, using iodine hypodermically in combination with chaulmoogra oil, obtained good results. In 1919, Dean combined the derivatives of chaulmoogra oil—the fatty acid group first isolated by Rogers—with iodine, using a 2 per cent. iodine mixture hypodermically and a 5 per cent. iodine mixture internally, and gave added proof of the value of the iodine in the treatment of leprosy. I have frequently given iodine internally with the cacodylate of soda hypodermically, obtaining excellent results in selected types of incipient leprosy.

To obtain permanent curative results in leprosy it is just as essential to use iodine in combination with other recognized drugs as it is to use mercury and the iodides with arsphenamine in the treatment of syphilis. As in syphilis, it is self evident that the intensive treatment of leprosy should be carried out for at least three years, but in the latter the treatment should be strict hospitalization and supervision for an indefinite period.

ROENTGEN-RAY DOSAGE FROM THE PATHOLOGIC POINT OF VIEW

PRELIMINARY REPORT *

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COMPARISON OF CELLS

Acute and subacute inflammatory tissues are characterized by lymphocytes—round cells. They are the least resistant of all pathologic cells and are the most readily influenced by therapeutic measures.

Chronic inflammatory tissues are characterized by fibroblasts—connective tissue cells. They are more resistant and less readily influenced than the lymphocytes.

Granulomas are characterized by giant, plasma and epithelioid cells. They are more resistant and less readily influenced than the inflammatory cells.

Neoplasm elements vary according to the type of tissue from which they originate. Those of the highest type (epithelial and glandular) are the most resistant and least readily influenced of all pathologic cells.

Normal tissue elements are more resistant than pathologic. The resistance varies according to the age of the person, the part of body and the type of tissue of which they are a part.

RESPONSE OF THE CELLS TO THE ACTION OF THE ROENTGEN-RAY

The intensity and the duration of the response of the cells to the roentgen-ray are in proportion to the degree of their resistance, that is, the response is most intense and of the longest duration in the cells of least resistance.

After a roentgen-ray exposure, the resistance of all cells is influenced and their activity is proportionately affected. The more resistant cells recover in less time than those of less resistance. If the interval between the exposures is sufficiently long, all the cells will recover. After a second exposure, the activity of the cells that have not fully recovered, is more readily affected as their resistance has already been influenced. With each successive exposure, the resistance is more and more influenced and the activity is proportionately less and less maintained. When the accumulative effects at the point of saturation are reached, the cells become nonresistant and inactive. The rapidity with which the point of saturation is reached depends on the character of

*From the Dermatological Department, Vanderbilt Clinic, New York.

the cells and the intensity of the exposures. It may result from a single exposure or from many exposures. When this stage is reached, involution sets in.

Involution.—The nonresistant and inactive tissue elements are unable to withstand the action of the local tissue assisted by the body's protective forces and are absorbed. (The body's protective forces are the circulating fluids and phagocytes.) If the involution is within bounds, normal absorption results. If it is rapid, ulceration may result. If normal tissue is involved, either ulceration or atrophy may result, depending on the rapidity of the absorption.

INTENSITY AND INTERVALS OF ROENTGEN-RAY EXPOSURES

Suberythema Doses.—Three weeks after a scalp is exposed to one unfiltered skin unit, the hair falls—an indication of complete inhibition of the hair papillae cells. As all the tissues exposed to the roentgen-ray are influenced, the pathologic cells, if exposed to suberythema doses, must be in the same state of inhibition at this time. Six weeks after the exposure the hair grows again—an indication of complete recovery of the hair papillae cells. As the intensity and the duration of the response to the roentgen ray are in proportion to the resistance, the pathologic cells will not have recovered to the same degree in the same time. If a second exposure is made at the time of recovery of the normal cells, that is, four weeks after the first exposure, the activity of the pathologic cells will be more affected, as their resistance has already been influenced.

Massive Doses.—About ten days after lesions are exposed to one and one-quarter to two and one-half skin units, an erythema develops in the surrounding area—an indication of complete inhibition of all the tissues exposed. About six weeks after the exposure the erythema completely disappears—an indication of complete recovery of the normal tissue elements. As normal tissue elements have greater resistance than pathologic and, as the intensity and duration of the response are in proportion to the resistance, the pathologic elements will not have recovered to the same degree in the same time. If a second exposure is made at this time, before the pathologic cells have completely recovered, their activity will be more affected as their resistance has already been influenced.

Summary.—The massive dose must not be repeated until the erythema has completely disappeared, which is an indication of normal tissue recovery. No tissue should be exposed to more than one skin unit in four weeks, the time of normal tissue recovery. If the exposures are repeated before the normal tissue elements have completely recovered, they may be so influenced that they will be absorbed, resulting in either ulceration or atrophy.

DOSAGE

Massive Doses.—One and one-fourth to two and one-half skin units should be given; this dose should be repeated when the erythema has completely disappeared.

TABLE 1.—RESPONSE IN CELLS OF LEAST RESISTANCE

Dose	Incomplete Recovery
Fractional doses, $\frac{1}{4}$ skin unit repeated every week	Acute and subacute inflammatory tissues.
Fractional doses, $\frac{1}{2}$ skin unit, repeated every two weeks	Acute and subacute inflammatory tissues; chronic inflammatory tissues.
Suberythema doses, 1 skin unit, repeated every four weeks	Acute and subacute inflammatory tissues; chronic inflammatory tissues; granuloma.
Massive doses, $1\frac{1}{4}$ to $2\frac{1}{2}$ skin units, repeated when erythema subsides	Acute and subacute inflammatory tissues; chronic inflammatory tissues; granuloma; neoplasm.

TABLE 2.—RESPONSE IN CELLS OF GREATEST RESISTANCE

Dose	Complete Recovery
Fractional doses, $\frac{1}{4}$ skin unit repeated every week	Normal; neoplasm; granuloma; chronic inflammatory tissues.
Fractional doses, $\frac{1}{2}$ skin unit, repeated every two weeks	Normal; neoplasm; granuloma.
Suberythema doses, 1 skin unit, repeated every four weeks	Normal; neoplasm.
Massive doses, $1\frac{1}{4}$ to $2\frac{1}{2}$ skin units, repeated when the erythema subsides	Normal.

Neoplasms, characterized by cells similar to those from which they originate, are exposed, according to their type, to a varying dose of from one and one-fourth to two and one-half skin units. After the erythema has subsided, usually in about six weeks, an involution of the lesion is sometimes noted. After repeated exposures, the involution is more marked and more rapid. The procedure is maintained until the lesions are entirely absorbed. An atrophy and sometimes telangiectasis are noted in the areas exposed. If the exposures are repeated before the erythema completely disappears, an ulceration may result. If exposed to one unit or less, the neoplasm cells recover during the intervals, and the new growth is not influenced.

Suberythema Doses.—Suberythema doses of one skin unit should be repeated every four weeks. Granulomas, characterized by cells less resistant than those of neoplasms, are exposed to one unit repeated every four weeks until complete involution results. If exposed to less than one unit, these cells recover and the lesions are not influenced.

Fractional Doses.—These consist of one-half skin unit repeated every two weeks. Chronic inflammatory tissues, characterized by cells

less resistant than those of granulomas, are exposed to half the dose in half the time, that is, one-half skin unit repeated every two weeks until complete involution results.

Fractional doses of one-fourth skin unit are repeated every week. Acute and subacute inflammatory tissues, characterized by cells of least resistance, are exposed to doses not exceeding one-quarter skin unit per week, repeated weekly until complete involution results.

The total amount of roentgen-ray for granulomas, acute, subacute and chronic inflammatory tissues, must not exceed one skin unit in four weeks. If exposed to larger doses, the response may be so active that ulceration may result.

Neoplasms and granulomas are seldom free from inflammatory tissue elements. If neoplasms are exposed to less than massive doses, and granulomas to less than suberythema doses, involution in these lesions is sometimes noted. The degree of involution depends on the amount of lymphoid or connective tissue elements present as part of, or about, these pathologic processes.

RESPONSE OF CELLS

The response is most intense and of longest duration in the cells of least resistance. These cells do not completely recover during the intervals between the exposures.

The response is least intense and of shortest duration in the cells of greatest resistance. These cells recover completely during the intervals between the exposures.

As it is never the agent but the response of the living cells to the agent that is responsible for the therapeutic results, the least amount of rays necessary to produce these results in any given tissue should be employed. If the dose is too intense, that is, the amount is excessive, the response may be so active that ulceration may result. If the amount is insufficient, the cells recover during the intervals, and the lesion is not influenced.

EXPERIMENTAL PRODUCTION OF CLINICAL TYPES OF SYPHILIS IN THE RABBIT *

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Syphilis in the human subject is characterized by the occurrence of a succession of lesions of various types which follow one another in a more or less orderly progression from the chancre to the terminal stages of the infection, and while to each period of the infection certain types of lesions have been assigned, the order of their appearance is not entirely fixed nor can one say just what lesions may be expected to occur in a given case.

The factors that determine these features of the disease may be numerous, and the results of their action differ so widely that diversity rather than uniformity has come to be recognized as one of the most fundamental characteristics of syphilis. The causes which underly this diversity of clinical types are but little understood. It is of course obvious that there are two sets of factors which may contribute to this condition, namely, the reactive mechanism of the host and the disease producing properties of the organisms concerned.

Within recent years, the tendency has been to lay more and more stress on the influence of the latter group of conditions. The possibilities of the existence of so-called strains of *Spirochaeta pallida* was first suggested by Noguchi¹ and later made the subject of experimental investigations by Nichols,² Reasoner³ and others. More recently this idea has been emphasized by the work of Levaditi, Marie⁴ and their co-workers in connection with general paresis. As yet, however, the subject of the cause of clinical variation is an open one, and while syphilographers have recognized the fact that many peculiarities of the infection may be due to causes other than strain differences, this possibility has been more or less neglected by experimental investigators.

It is not easy to approach the problem of clinical variation by means of observation on the human subject, since such a small part of the phenomena of infection can be observed in an individual case, and neither the host nor the causative agent is subject to the necessary

* From the Laboratories of the Rockefeller Institute for Medical Research, New York.

1. Noguchi: J. Exper. Med. **15**:201, 1912.

2. Nichols: J. Exper. Med. **19**:362, 1914.

3. Reasoner: J. A. M. A. **67**:1799, 1916.

4. Levaditi and Marie: Ann. Int. Past. **33**:741, 1919. Marie, Levaditi and Banu: Compt. rend. Acad. d. Sc. **170**:1021, 1920.

measure of control. In the experimental animal, however, a large part of these difficulties are removable, and it is possible to reproduce many of the phenomena of the human infection under conditions of acceptable control. Thus by local inoculation into the testicles or scrotum of the rabbit, one may obtain an infection which begins with a primary lesion and after a lapse of from six to twelve weeks, is marked by the appearance of a variety of lesions in other parts of the body, together with a general lymphadenitis and at times by constitutional disturbances; there are lesions of the skin and appendages, the mucous membranes, the periosteum and bones, and of the eyes. The infection is not identical with that in man but the analogy is sufficiently close for one to make comparisons, and, at the same time, the differences are sufficiently great to enable one to make clear-cut experimental distinctions.

Variation in the clinical course of the disease is characteristic of the animal, as it is of the human, infection, and there are, as we have said, two aspects of the problem of variation, only one of which has been dealt with from an experimental standpoint. The subject of variation is an intricate one and at this time we do not propose to consider the ultimate possibilities of either of the potential factors concerned.

It has been noted, however, that with the use of a given strain of *Spirochaeta pallida*, one may still obtain infections which exhibit decided clinical variations, not only in the type of lesions which appeared in a given group of tissues, but equally so in the groups of tissues involved and this is of more fundamental importance. An analysis of the circumstances under which such variations occurred showed an appreciable connection between the experimental conditions employed and the type of infection produced. This was especially noticeable in the frequency with which keratitis and iritis occurred following the use of one set of conditions and the frequency with which lesions of the periosteum and bone followed another.

Previous experiments had shown that, while generalized lesions occurred in only a small percentage of rabbits inoculated by certain methods, it was possible to modify the course of the infection to such an extent that the occurrence of generalized lesions became the rule rather than the exception.⁵ This work was founded on a modified conception of the theory of inhibition. That the development of a lesion in one testicle was capable of inhibiting the development of other lesions in the rabbit was first demonstrated by Nichols⁶ in connection with metastatic lesions of the testicles and applied by him in

5. Brown and Pearce: Arch. Dermat. & Syph., 1920, **11**:675.

6. Nichols, H. J.: J. Exper. Med. **14**:211, 1911.

an explanation of the phenomena of relapse in human syphilis with especial reference to neurorecidives.⁷

Realizing the importance of the influence which the primary reaction exerted on the character of the infection in the rabbit, we were first able to convert a local into a general disease by diminishing or suppressing the testicular reaction. With a knowledge of what had been accomplished in this respect, it appeared that one might go a step further and, by modifying the defensive reaction in different ways, produce types of disease that would conform to alterations in the mechanism of animal resistance, the infecting organism being maintained as a constant factor in the reaction.

EXPERIMENTAL MODIFICATION OF THE INFECTION

Experiments that have been carried out show that definite type alterations can be produced in response to the use of experimental procedures which influence the reaction to infection. The character of the changes and the manner in which they were obtained may be illustrated by the following experiment:

Forty-four rabbits were inoculated in the testicles with the Nichols strain of *Spirochaeta pallida*, using for each testicle 0.5 c.c. of an emulsion containing numerous spirochetes, as many as four to eight to the microscopic field. The animals were divided equally into two series, A and B. Those of Series A were inoculated in both testicles and those of Series B in only one testicle. Lesions were palpable in the testicles at from ten to fourteen days after inoculation. Each series was then further divided into four groups, making each group as nearly comparable to the others of the series as possible from the standpoint of the animals and the state of the testicular infection. The several groups were handled as follows:

Group 1; Controls; Six Animals.—The infection in this group of animals was permitted to progress without interference of any kind.

Group 2; Early Castration; Five Animals.—These animals were castrated fourteen days after inoculation. In Series A, both testicles were removed; in Series B, only the infected testicle was removed.⁸

Group 3; Late Castration; Five Animals.—Castration was carried out as in Group 2, twenty-eight days after inoculation.

Group 4; Therapeutic Suppression of Testicular Reaction; Six Animals.—These animals were given a single intravenous injection of arsenophenylglycyl dichloro-m-aminophenol for the purpose of temporarily suppressing the reaction in the testicle and of lowering the animal resistance.

All animals were kept under observation for from three to three and a half months after inoculation. During this time, they were examined almost daily and full records of the progress of the infection were kept.

7. Nichols, H. J.: J. A. M. A. **63**:466, 1914.

8. All operations were done under ether anesthesia.

The purpose of some of these procedures may require a brief explanation. Early castration was employed as a means of aborting the testicular reaction early in the course of the infection and thus shifting the defensive reaction to other tissues before any considerable degree of protection had been developed. The use of late castration, on the other hand, represented an attempt to permit the infection to progress to a point at which the protection developing from the primary foci was nearly, but not quite, sufficient to prevent the occurrence of lesions in other parts of the body. The success of this attempt hinged on the judgment of the proper time at which to intervene, and castration was performed as the first cycle of testicular reaction was nearing completion. The progress of the infection was, of course, not uniform in all animals, and the time fixed for castration was based on the average animal of the group; this was too early in some cases and too late in others, but such irregularities could not be avoided if a constant time element were to be maintained.

The use of a therapeutic agent in this series of experiments was intended to accomplish more than a temporary restraint on the primary lesions. The effects produced by such agents are not entirely measurable by the reduction which they produce in existing lesions and, while we cannot discuss the action of therapeutic agents, it is necessary to state that in addition to any effect which may be attributable to a temporary suppression of existing lesions, therapeutic agents frequently nullify any protection that has been developed and render subsequent reactions on the part of the animal less effectual. It was for this purpose that arsenophenyglycyl dichloro-m-aminophenol was used.

The period of observation chosen was fixed with a view to including only one cycle of general reaction. Clinical relapse is prone to occur in the animal as in the human subject, and the inclusion of this class of phenomena would introduce more complex elements, which cannot be considered in this article.

RESULTS OBTAINED

The influence which these procedures exerted on the course and character of the infection may be learned from a comparison of the case incidence and relative severity of generalized lesions, the groups of tissues involved, the order of involvement and the time after inoculation at which the lesions appeared. For convenience, these facts have been tabulated in parallel columns in the table. The list of conditions given includes no lesions of uncertain or doubtful character. When any doubt existed, the condition was recorded as suspicious or doubtful, as the case might be, and animals showing such affections are marked with an asterisk (*).

As one examines the data recorded in the table, the first thing to be noted is that the occurrence and the severity of generalized lesions among animals of a given group was inconstant. This indicates the existence of a variable in the reaction of individual animals to a given set of conditions which must be regarded as present in all cases.

EFFECT PRODUCED ON THE CHARACTER OF THE INFECTION BY MODIFYING THE REACTION OF THE HOST IN ANIMALS INOCULATED WITH A CONSTANT DOSE OF A GIVEN STRAIN OF SPIROCHAETA PALLIDA

Series A: Bilateral Inoculations			Series B: Unilateral Inoculations		
Number and Group	Generalized Syphilis	Lesions in Order of Their Appearance, Time in Days	Number and Group	Generalized Syphilis	Lesions in Order of Their Appearance, Time in Days
Group 1A			Group 1B		
1	—*		1	—*	
2	—		2	++	S.(57,78) E.(78)
3	—		3	—*	
4	—*		4	++	P.B.(55) E.(78,84)
5	—		5	—	
6	+	S.(57)	6	++++	S.(57,71) P.B.(63)
Group 2A			Group 2B†		
1	—*		1	++	P.B.(50)
2	++	S.(28) MM.(41)	2	++	MM.(41) P.B.(73,78)
3	—		3	+	P.B.(57)
4	++	P.B.(79) S.(89)	4	++	P.B.(41,57) S.(57)
5	+++	P.B.(57,78) S.(79) E.(85)			
Group 3A			Group 3B†		
1	++	P.B.(57) S.(71)	1	+	MM.(63)
2	—*		2	—	
3	+++	S.(29) MM.(63) E.(80,84)	3	+++	P.B.(50) S.(50,76)
4	+	E.(85)	4	—*	
5	++	S.(50) E.(65)			
Group 4A			Group 4B		
1	+	P.B.(63) S.(71,78,80)	1	++	P.B.(55) S.(90)
2	+	P.B.(57) *	2	+++	P.B.(55,57)
3	—*		3‡	+	P.B.(47)
4	+++	P.B.(50) S.(50,57) MM.(71)	4	++	P.B.(55) E.(97)
5	++	P.B.(41)	5	++	S.(35) P.B.(59)
6	++	P.B.(71,78)	6	++	S.(63) MM.(97)

— Negative

+ Slight infection

++ Moderate infection

E., eyes; MM., mucous membranes and mucocutaneous borders; P.B., periosteum and bone; S., skin.

* Animals showing suspicious lesions, not definite.

† One animal in each of these groups died before results could be determined.

‡ The animal developed symptoms of acute meningitis as the first lesions were appearing and was anesthetized and killed. Spirochetes were recovered from the cerebrospinal fluid. There was no bacterial infection.

Figures in parentheses () give the time in days in which the lesions appeared.

Considering the character of the infection which occurred under the several conditions employed, it will be seen that it varied from an infection in which scarcely any lesions were demonstrable (except those in the testicles), as in Group 1 A, to infections in which a variety of generalized lesions occurred in practically all the animals of the group. This is the first respect in which it can be seen that a modification in the type of the infection was produced.

The next condition to be noted is that the character of the disease among the animals of a given group also varied. In Group 1 B, for example, there was one case of skin and eye infection, another of bone and eye infection and a third of skin and bone infection; or, there were two cases each of skin, bone and eye infection. A similar condition prevailed in Group 2 A but in 2 B a different type of result was obtained. Here there was an unbroken series of cases of bone syphilis, two of the four animals showing skin or mucous lesions as well.

That the occurrence of such a group of infections cannot be regarded as a coincidence is shown by the fact that when analogous conditions were employed in Groups 4 A and B, the same type of infection was again produced. Further than this, a distinctly different type of infection was produced in the animals of Group 3 A by permitting the testicular reaction to progress much longer before suppression was attempted. In only one of the four animals in this group did bone lesions occur as contrasted with its occurrence in all of those of Groups 2 B and 4 A, and five of the six animals in 4 B. The infection in Group 3 A was preeminently one of skin and eyes; three of the animals showed skin lesions and three of them eye lesions and in one the eye lesions were the only lesions present.

The prominence of the latter type of infection is not fully brought out in this series of experiments, which covered only a little more than three months. This, as we realized, did not afford a proper opportunity for the development of eye lesions, which are rarely seen until toward the end of the third month and which tend to occur later when other conditions are most marked. Skin lesions showed the same tendency to late appearance under similar circumstances, and late lesions would doubtless have been more numerous had the period of observation been longer. The occurrence of these late lesions would not have altered the general type of the infection, however, but would merely have served to emphasize the conditions described.

In contrasting the manifestations of syphilis in the rabbit with those of man, attention should be called to two conditions: First, that the disease in the rabbit is not entirely comparable either to the acquired or the congenital form of the human infection, but presents an interesting combination of the two conditions. In the second place, the most noticeable difference in the sequence of tissue involvement is the position occupied by skin and bone infections, which is the reverse of that in man (acquired syphilis). This is to be accounted for by the fact that in the rabbit the skin is a furred coat, and for the most part, is less subject to infection or to the action of a host of conditions which predispose to skin infection than is the skin of man.

CLINICAL TYPES OF DISEASE

The fact that it is possible to produce a scale of variations in the clinical course of syphilitic infections by modifying the reaction of the experimental animal, indicates the importance of this group of factors in determining the character of the disease. It also suggests that each group of tissue reactions, or lesions, bears some relation to the reactions or lesions of other tissues and, therefore, to the course of the disease as a whole.

We shall not attempt to give a detailed statement of these relationships, but the simplest explanation which can be offered for the results reported is one which is based on inherent tissue susceptibility and tissue reactivity.

In the first place, the occurrence or nonoccurrence of generalized lesions in the rabbit, as well as the character of these lesions, appears to depend primarily on a protective reaction which takes place at the primary foci of infection and to some extent on the relative susceptibility of other tissues. It is difficult to say what part the latter condition plays in determining the general course of the disease, but unless a given tissue furnishes suitable conditions for the growth and multiplication of the spirochetes, no very active lesions are likely to occur, nor will the reaction in such tissues contribute materially to the defensive mechanism either locally or generally.

In the second place, it is conceivable that the protection developed from a given source may not affect all tissues, or even all parts of the body, in an equal degree or at the same rate, but that it may be extended progressively from the primary lesions to successive tissue groups, being sufficient to protect one group of tissues at a time when little or no protection is afforded to another.

According to this conception, the tissues which become involved or the lesions which develop in any given case would represent a measure of the effectiveness and the state or progress of the reaction in that animal. That such may be the case is indicated by the fact that certain groups of tissues tend to become involved in a given order; thus, bone lesions, if they occur at all, tend to follow those of the testicles or scrotum, while keratitis and iritis occur toward the end of the cycle of tissue involvement, the skin and mucous membranes occupying an intermediate position. Further than this, it has been shown that by early and radical interference, it is possible to so alter the course of the disease as to cause bone lesions practically to supplant those of the testicle in the defensive reaction; conversely, by permitting the testicular reaction to progress to a given point, it is possible to confer protection on this group of structures. In this case no bone lesions occur, but the generalized disease begins with involvement of the next group of tissues in order, producing an infection which is essentially one of the skin, mucous membranes and eyes.

Going still further, it is found that while, in the majority of animals inoculated in both testicles a high degree of protection seems to be conferred on other tissues of the body, in many instances, the protection fails to reach the eyes, lesions of the cornea and iris appear as the only clinical manifestations of a generalized disease.

This fact, taken in conjunction with other circumstances surrounding eye infections, is of especial interest on account of a point of view which is introduced toward certain manifestations of syphilis, especially neurosyphilis. In the rabbit, eye lesions are not only terminal and frequently the only generalized conditions that occur, but they are also relatively slight and more prone to repeated relapse than any other class of lesions. In the light of the conditions reported in the foregoing, these circumstances suggest that all tissues are not equally protected by the general reaction which occurs during the early stages of a syphilitic infection and that certain tissues which fail to receive this protection, although less susceptible to injury or infection than other tissues, may be capable of only a relatively slight degree of self-protection. This is undoubtedly the case in the experimental animal, and if similar conditions obtain in man, such conditions as neurosyphilis may be explainable on this basis.

It was the peculiar chain of circumstances surrounding eye infections which first drew our attention to the possibility of establishing the existence of a definite sequence of defensive reactions in the experimental animal with its corollary of a sequence in tissue protection and the possibility of producing infections of different types by modifying the defensive reaction at its source. The type of infection produced, therefore, by the inoculation of a given strain of *Spirochaeta pallida*, may be regarded as a resultant of the operation of the several factors indicated and subject, through this cause alone, to a wide degree of variation.

SUMMARY AND CONCLUSIONS

In the course of investigations dealing with generalized syphilis in the rabbit, it was noted that distinctly different types of disease were frequently produced by inoculations made with a given strain of *Spirochaeta pallida*; it also appeared that there was an appreciable connection between the experimental conditions employed and the type of disease which occurred.

Since it had been found possible to convert a disease which is usually localized into a generalized disease by diminishing or suppressing the primary reaction, it appeared that by modifying the reaction in different ways, one might produce types of disease which would conform to alterations in the defensive mechanism. Experiments carried out on a large series of animals showed that such was the case. By various

experimental procedures, different types of infection were produced, and in this way it was found that there was a definite sequence of tissue involvement or of tissue reactions which made it possible to produce infection or to confer protection on a given group of tissues according to the nature of the means employed.

From the manner in which the infection responded to modifications of the defensive reaction, the conclusion was drawn that a wide variation in the clinical type of the disease might be traceable to this one group of causes. This, of course, does not eliminate the possibility that variation in the biologic properties of the infecting organisms may contribute to further variations in the type of the disease.

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A STUDY OF ARSPHENAMIN-SERUM PRECIPITATES
AND THEIR RELATION TO CLINICAL
REACTIONS *

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Of the numerous theories advanced in explanation of the reactions and fatalities following the intravenous injection of solutions of arspenamin, considerable attention has been given to those based on the formation of precipitates in the blood which may result in pulmonary embolism and the production of immediate symptoms and even death.

REVIEW OF LITERATURE

As early as 1911, Michaelis¹ suggested that precipitates found in the blood in vivo may be responsible for fatalities following the intravenous injection of arspenamin and a little later Miessner² showed that mixtures of acid solutions of arspenamin and defibrinated blood or horse serum in test tubes produced heavy precipitates. When an alkaline solution of arspenamin was used, he failed to obtain these precipitates. Schottmüller³ reported the same results from mixtures in vitro of acid and of alkaline solutions of arspenamin and blood plasma. Both Miessner and Schottmüller suggested that these precipitates may have been the cause of death in certain instances following the intravenous injection of acid solutions of arspenamin. In an extensive series of experiments with rabbits and dogs, Joseph⁴ corroborated Miessner's observations that acid but not alkaline solutions produced precipitates when mixed with blood in test tubes, and that the intravenous injection of acid solutions produced precipitates in the venous blood which collected in the right side of the heart and in the lungs.

* From the Dermatological Laboratories of Philadelphia.

* This investigation was aided by funds accruing from the preparation of arspenamin.

1. Michaelis, L.: Die Ehrlich-Hata Behandlung in der inneren Medizin. Deutsch. med. Wchnschr. **36**:2278, 1910.

2. Miessner: Die Ursache für die giftige Wirkung saurer Salvarsanlösungen. Deutsch. med. Wchnschr. **37**:491, 1911.

3. Schottmüller: Deutsch. med. Wchnschr. **37**:670, 1911.

4. Joseph, D. R.: On the Formation of Precipitates After the Intravenous Injection of Salvarsan. J. Exper. Med. **14**:83, 1911.

The composition of these precipitates has also been a subject of much interest; Fleig⁵ regarded them as precipitated proteins, while Danysz,⁶ who more recently has expounded these theories of precipitation, believes that the precipitates are largely composed of the insoluble arsphenamin base or insoluble compounds of the base in combination with calcium phosphates.

Berman⁷ regards the precipitates as composed of proteins and suggests that an increased protein content of the blood in certain syphilitic patients may favor precipitation in vivo, even of properly alkalized solutions of arsphenamin. Berman analyzed the blood of two patients by the nephelometric method of Kober and Graves and found an increased protein content, essentially of the globulins. Furthermore, the serums of eleven patients, among 300 injections, who developed an immediate reaction following the intravenous injection of alkaline solutions of arsphenamin, produced heavy whitish yellow precipitates when mixed in test tubes with the arsphenamin solutions, whereas the serums of nonreacting subjects, according to Berman, did not. Berman states that by previously testing the serum and the solution of arsphenamin one could tell whether or not an immediate reaction (designated as the "nitritoid crisis") would follow the injection.

The investigations of Schamberg, Kolmer, Raiziss and Weiss⁸ essentially confirmed the observations of Miessner and Joseph that precipitates are produced only when acid or insufficiently neutralized solutions of arsphenamin are added to serum, plasma or defibrinated blood. Furthermore, they showed that solutions of neo-arsphenamin do not produce these precipitates but may nevertheless produce immediate reactions similar to those produced by arsphenamin when administered to human beings by intravenous injection. The precipitates formed in mixtures of blood and acid solutions of arsphenamin were found to be composed of arsphenamin which immediately dissolved on the addition of a weak alkali, such as decinormal solutions of sodium hydroxid.

5. Fleig, C.: *La toxicite de la salvarsan* (Monograph), Paris, 1914.

6. Danysz, J.: *Les proprietes physicochimiques des produits du groupe des arsenobenzenes leurs transformations dans l'organisme*, Ann. d. l'Inst. Pasteur **31**:114, 1917.

7. Berman, L.: *The Nitritoid Crises After Arsphenamin Injections*, Arch. Int. Med. **22**:217, 1918.

8. Schamberg, J. F.; Kolmer, J. A.; Raiziss, G. W., and Weiss, C.: *Laboratory and Clinical Studies Bearing on the Causes of the Reactions Following Intravenous Injections of Arsphenamin and Neo-Arsphenamin*, Arch. Dermat. & Syph. **1**:235, 1920.

PURPOSES OF INVESTIGATION

The chief purpose of this investigation has been to study the serums, by Berman's technic, of those persons showing reactions while being treated for syphilis with intravenous injections of arsphenamin and neo-arsphenamin.

Berman's work was based on a study of the serums of eleven persons who showed a reaction (designated by Milian as the "nitritoid crisis") during, or immediately after, the intravenous injection of arsphenamin and characterized by redness of the face, dyspnea, a feeling of anguish and distress, cough and precordial pain. Our investigation has included a study of the serums, not only of patients showing these immediate reactions, but likewise the serums of patients showing the symptoms of early reactions, as designated by Schamberg, Kolmer and Raiziss,⁹ and characterized by chilliness or a distinct rigor, headache, vertigo, nausea, vomiting, diarrhea and rise of temperature developing within an hour or two or any time within twenty-four hours, after the intravenous injection of arsphenamin or neo-arsphenamin.

In this investigation we have confined ourselves to a study of the reactions described by Berman following the mixing of serums and solutions of arsphenamin in test tubes in relation to the clinical reaction; special studies on the proteins of the serums of syphilitic patients have been made by one of us (Tokuda), employing a refractometric method, the results being given in a separate communication.

TECHNIC

Blood was collected from a series of patients before the intravenous injections of arsphenamin or neo-arsphenamin were made, and the serums were tested with monosodium and disodium solutions of arsphenamin and solutions of neo-arsphenamin. Acid solutions of arsphenamin were not employed because every serum shows a heavy precipitate when mixed with these.

The solutions of arsphenamin used in the tests were 2 per cent. and of neo-arsphenamin 4 per cent. The monosodium solutions of arsphenamin were prepared by adding just enough sodium hydroxid to "clear" the solution after the precipitate had formed; the disodium solutions were prepared by adding one third excess of alkali after the solution had been "cleared."

The tests were conducted by placing 0.5 c.c. fresh unheated serum in three small test tubes and adding 0.5 c.c. of the monosodium and disodium solutions of arsphenamin and the solution of neo-arsphenamin

9. Schamberg, J. F.; Kolmer, J. A., and Raiziss, G. W.: Experimental and Clinical Studies of the Toxicity of Dioxydiamino-Arsenobenzene Dichlorhydrate, *J. Cutan. Dis.* **35**:286, (May-June) 1917.

to numbers 1, 2 and 3, respectively; controls were included in each set of tests in which saline solution replaced serum. The reactions were read at once and again one hour after standing at room temperature and recorded thus: — indicates that the mixtures remained clear; + indicates that the mixtures became opalescent; ++ indicates that the mixtures became turbid, and +++ indicates that the mixtures became turbid with the production of a whitish yellow precipitate.

The patients were given intravenous injections of monosodium arspenamin (just enough alkali to clear the solution), each 0.1 gm. being dissolved in about 20 c.c. of whitish water. The neo-arsphenamin was administered in dilute solutions and also in concentrated solutions by means of a syringe.

The "immediate reactions" referred to were observed in the clinic during, or immediately after, the injections. For the "early reactions" we were obliged to accept the statements of patients who left the clinic without symptoms but reported on furnished blanks the subsequently developing symptoms previously mentioned and classified under the "early reaction."

RESULTS

The results are summarized in Tables 1, 2, 3, 4 and 5.

While this study was being made no "immediate reactions" or "nitritoid crises" were observed during the administration of arspenamin, but sixteen patients developed these reactions during the administration of neo-arsphenamin. The serum reactions are shown in Table 1.

TABLE 1.—RESULTS WITH THE SERUMS OF SIXTEEN PATIENTS SHOWING IMMEDIATE REACTIONS DURING THE INTRAVENOUS INJECTION OF NEO-ARSPHENAMIN

Compound Administered	Serum Reactions With Monosodium Arspenamin		Serum Reactions With Disodium Arspenamin		Serum Reactions With Neo-arsphenamin	
	At Once	After One Hour	At Once	After One Hour	At Once	After One Hour
No. 493	—*	++	—	—	—	—
No. 498	—	++	—	—	—	+
No. 518	++	++	—	+	—	+
No. 506	++	++	—	—	—	—
No. 544	—	—	—	—	—	—
No. 566	—	—	—	—	—	—
No. 541	—	—	—	—	—	—
No. 585	+	+++	—	—	—	—
No. 585	—	—	—	—	—	—
No. 589	—	—	—	—	—	+
No. 620	—	—	—	—	—	+
No. 641	—	—	—	—	—	—
No. 641	—	—	—	—	—	—
No. 654	—	—	—	—	—	—
No. 667	—	—	—	—	—	—
No. 651	—	—	—	—	—	+

* — indicates that mixtures of serum and arspenamin solution were perfectly clear; +, opalescent; ++, turbid; +++, very turbid with precipitate.

Ten patients developed "early reactions" following the intravenous injection of arspenamin. The serum reactions are given in Table 2.

TABLE 2.—RESULTS WITH THE SERUMS OF TEN PATIENTS SHOWING EARLY REACTIONS FOLLOWING THE INTRAVENOUS INJECTION OF ARSPHENAMIN

Compound Administered	Serum Reactions With Monosodium Arspenamin		Serum Reactions With Disodium Arspenamin		Serum Reactions With Neo-arsphenamin	
	At Once	After One Hour	At Once	After One Hour	At Once	After One Hour
No. 3586	—*	—	0	0	0	0
No. 3586	—	—	—	—	—	—
No. 3592	—	++	—	—	—	—
No. 3592	—	++	—	—	—	—
No. 3592	—	—	—	—	—	—
No. 3592	—	—	—	—	—	—
No. 3592	—	—	—	—	—	—
No. 3605	—	++	—	—	—	—
No. 3605	—	++	—	—	—	—
No. 3605	—	++	—	—	—	—

* — indicates that mixtures of serum and arspenamin solution were perfectly clear; +, opalescent; ++, turbid.

Twenty-five patients developed "early reactions" following the intravenous injection of neo-arsphenamin. The serum reactions are given in Table 3.

TABLE 3.—RESULTS WITH THE SERUMS OF TWENTY-FIVE PATIENTS SHOWING EARLY REACTIONS FOLLOWING THE INTRAVENOUS INJECTION OF NEO-ARSPHENAMIN

Compound Administered	Serum Reactions With Monosodium Arspenamin		Serum Reactions With Disodium Arspenamin		Serum Reactions With Neo-arsphenamin	
	At Once	After One Hour	At Once	After One Hour	At Once	After One Hour
No. 487	—*	—	0	0	0	0
No. 487	—	—	—	—	—	—
No. 468	—	—	—	—	—	—
No. 493	—	++	—	—	—	—
No. 518	—	+	—	—	—	—
No. 499	—	+	—	—	—	—
No. 499	—	++	—	—	—	—
No. 509	—	++	—	—	—	—
No. 509	—	++	—	—	—	—
No. 519	—	+	—	—	—	—
No. 521	—	+	—	—	—	—
No. 497	+	++	—	—	—	—
No. 518	+	++	—	—	—	—
No. 526	+	++	—	—	—	—
No. 526	+	++	—	—	—	—
No. 533	—	+	—	—	—	—
No. 533	+	++	—	—	—	—
No. 544	+	++	—	—	—	—
No. 544	+	++	—	—	—	—
No. 533	+	++	—	—	—	—
No. 538	+	++	—	—	—	—
No. 547	+	++	—	—	—	—
No. 558	+	++	—	—	—	—
No. 544	—	—	—	—	—	—
No. 574	—	—	—	—	—	—

* — indicates that mixtures of serum and arspenamin solution were perfectly clear; +, opalescent; ++, turbid.

Table 4 gives the serum reactions of twenty-five patients who did not show any symptoms of reactions after the intravenous injection of arsphenamin; Table 5 gives the serum reactions of sixty-six patients who did not show any symptoms after the administration of neo-arsphenamin. Both tables are introduced as controls.

TABLE 4.—RESULTS WITH THE SERUMS OF TWENTY-FIVE PATIENTS WHO DID NOT SHOW ANY REACTIONS AFTER THE ADMINISTRATION OF ARSPHENAMIN

Compound Administered	Serum Reactions With Monosodium Arsphenamin		Serum Reactions With Disodium Arsphenamin		Serum Reactions With Neo-arsphenamin	
	At Once	After One Hour	At Once	After One Hour	At Once	After One Hour
No. 3570	—*	—	—	—	—	—
No. 3570	—	—	—	—	—	—
No. 3570	—	—	—	—	—	—
No. 3570	—	—	—	—	—	—
No. 3570	—	—	—	—	—	—
No. 3586	+	++	—	—	—	—
No. 3586	+	+++	—	—	—	—
No. 3586	+	+++	—	—	—	—
No. 3586	+	+++	—	—	—	—
No. 3570	—	++	—	—	—	—
No. 3570	—	++	—	—	—	—
No. 3570	—	+	—	—	—	—
No. 3570	—	++	—	—	—	—
No. 3592	—	++	—	—	—	—
No. 3592	—	+++	—	—	—	—
No. 3592	—	+++	—	—	—	—
No. 3592	—	—	—	—	—	—
No. 3605	—	+	—	—	—	—
No. 3605	—	+	—	—	—	—
No. 3605	—	+	—	—	—	—
No. 3605	+	+++	—	—	—	—
No. 3605	+	+++	—	—	—	—
No. 3605	+	+++	—	—	—	—
No. 3530	—	+	—	—	—	—
No. 3530	—	+	—	—	—	—

* — indicates that mixtures of serum and arsphenamin solution were perfectly clear; +, opalescent; ++, turbid.

These results are summarized in Table 6 which shows at a glance the percentages of positive serum reactions with the different solutions of arsphenamin and neo-arsphenamin. In preparing this table, only ++ and +++ reactions developing at once with the solutions of arsphenamin have been included as possibly possessing some significance and corresponding to the reactions described by Berman. As stated by Berman, + reactions (opalescence) may be excluded. Reactions developing after the mixtures have stood one hour are likewise of little significance as this phenomenon has been found so frequently with normal serums and the serums of lower animals.

Since mixtures of solutions of neo-arsphenamin and serum are usually perfectly clear even after standing one hour, positive reactions may be of some significance and are included.

TABLE 5.—RESULTS WITH THE SERUMS OF SIXTY-SIX PATIENTS WHO DID NOT SHOW ANY REACTIONS AFTER THE ADMINISTRATION OF NEO-ARSPHENAMIN

Compound Administered	Serum Reactions With Monosodium Arspenamin		Serum Reactions With Disodium Arspenamin		Serum Reactions With Neo-arsphenamin	
	At Once	After One Hour	At Once	After One Hour	At Once	After One Hour
No. 487	—	—	—	—	—	—
No. 487	—	—	—	—	—	—
No. 487	—	—	—	—	—	—
No. 487	—	—	—	—	—	—
No. 468	—	—	—	—	—	—
No. 468	—	—	—	—	—	—
No. 487	—	—	—	—	—	—
No. 484	++	++	—	—	—	—
No. 484	++	++	—	—	—	—
No. 484	++	++	—	—	—	—
No. 484	+	++	—	—	—	—
No. 484	+	++	—	—	—	—
No. 465	+	++	—	—	—	—
No. 465	+	++	—	—	—	—
No. 459	—	+	—	—	—	—
No. 459	—	+	—	—	—	—
No. 503	—	++	—	—	—	—
No. 493	—	++	—	—	—	—
No. 506	—	+	—	—	—	—
No. 509	—	+	—	—	—	—
No. 512	—	+	—	—	—	—
No. 518	—	+	—	—	—	—
No. 518	—	+	—	—	—	—
No. 518	—	+	—	—	—	—
No. 499	—	+	—	—	—	—
No. 353	—	+	—	—	—	—
No. 509	—	+	—	—	—	—
No. 509	—	+	—	—	—	—
No. 521	—	+	—	—	—	—
No. 521	—	+	—	—	—	—
No. 518	++	++	—	—	—	—
No. 506	++	++	—	—	—	—
No. 526	—	+	—	—	—	—
No. 529	—	+	—	—	—	—
No. 529	—	+	—	—	—	—
No. 533	—	+	—	—	—	—
No. 533	—	++	—	—	—	—
No. 533	—	++	—	—	—	—
No. 533	—	++	—	—	—	—
No. 533	—	—	—	—	—	—
No. 538	—	+	—	—	—	—
No. 538	—	+	—	—	—	—
No. 538	—	+	—	—	—	—
No. 523	—	++	—	—	—	—
No. 554	+	++	—	—	—	—
No. 554	+	++	—	—	—	—
No. 554	+	++	—	—	—	—
No. 538	+	++	—	—	—	—
No. 538	+	++	—	—	—	—
No. 544	+	++	—	—	—	—
No. 544	++	++	—	—	—	—
No. 558	++	++	—	—	—	—
No. 547	++	++	—	—	—	—
No. 547	+	++	—	—	—	—
No. 547	+	++	—	—	—	—
No. 541	+	++	—	—	—	—
No. 541	+	++	—	—	—	—
No. 562	—	+	—	—	—	—
No. 533	—	+	—	—	—	—
No. 544	—	—	—	—	—	—
No. 550	—	—	—	—	—	—
No. 550	—	+	—	—	—	—
No. 570	—	—	—	—	—	—
No. 566	—	—	—	—	—	—
No. 574	—	—	—	—	—	—

* — indicates that mixtures of serum and arspenamin solution were perfectly clear; +, opalescent; ++, turbid.

TABLE 6.—SUMMARY SHOWING PERCENTAGES OF SERUMS YIELDING TURBID REACTIONS AT ONCE WHEN MIXED WITH SOLUTIONS OF ARSPHENAMIN AND OPALESCENT REACTIONS WITHIN ONE HOUR WHEN MIXED WITH SOLUTIONS OF NEO-ARSPHENAMIN

Reactions	Number Tested	Percentages of Positive Serum Reactions With		
		Monosodium Arspenamin	Disodium Arspenamin	Neo-arsphenamin
Immediate reactions after neo-arsphenamin.....	16	12	—	31
Early reactions after arspenamin.....	10	—	—	—
Early reactions after neo-arsphenamin.....	25	—	—	—
No reactions after arspenamin.....	25	—	—	—
No reactions after neo-arsphenamin.....	66	11	—	5

SUMMARY

1. The amount of alkali in the solutions of arspenamin has great influence on the reactions following the mixture of a serum and arspenamin in test tubes. For this reason the solutions of monosodium arspenamin produce more precipitates than the disodium solutions because the latter contain an excess of alkali. Furthermore, all precipitates, including those produced when acid solutions of arspenamin are mixed with serums, can be dissolved at once by the addition of a few drops of a normal solution of sodium hydroxid. This constitutes proof that the precipitate is a drug precipitate and not a protein precipitate, because a protein precipitate could not be redissolved in this manner.

2. The amount of alkali in the solutions of neo-arsphenamin may have a similar relation to the results observed when solutions are mixed with serums. The results observed in these experiments indicated that the solution of some lots of neo-arsphenamin produced more positive reactions than other lots; furthermore, the addition of a single drop of normal sodium hydroxid immediately dissolved the precipitates and yielded clear solutions.

3. The serums of patients exhibiting immediate (nitritoid) reactions after neo-arsphenamin did not form precipitates when brought in contact, in the test tube, with solutions of neo-arsphenamin. Negative results were similarly obtained with the serums of patients who had febrile and gastro-intestinal reactions.

4. Test tube precipitates of arspenamin occurred as frequently and as pronouncedly with the serums of patients not exhibiting febrile and gastro-intestinal reactions after arspenamin as with the serums of those who did manifest such reactions. As practically no nitritoid reactions occurred after arspenamin during the period of our study, the serums of such patients could not be tested.

5. In so far as the results observed with the serums of patients showing immediate (nitritoid) reactions after the administration of neo-arsphenamin are concerned, we found no evidence to support the deductions of Berman that these simple tests will serve to foretell the occurrence of these reactions, although it must be stated that Berman's tests were conducted with the serums of patients who had "nitritoid" reactions after the administration of arsphenamin.

6. It is highly probable that the reactions observed when serums and solutions of arsphenamin and neo-arsphenamin are mixed in test tubes, are primarily dependent on the amount of alkali present in the solutions or in the serums. The amount of alkali present in different lots of arsphenamin and neo-arsphenamin is likely to vary and thereby influence the occurrence of precipitates with different lots of the drugs and the serums of patients. These precipitates are largely composed of arsphenamin or neo-arsphenamin rather than of serum proteins, and are readily dissolved by the addition of traces of sodium hydroxid.

A STUDY OF THE SPINAL FLUID IN ONE THOUSAND EIGHT HUNDRED AND SIXTY-NINE CASES OF SYPHILIS IN ALL STAGES

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In 1913, with the installation of the syphilis clinic at the University of Michigan, a study of the spinal fluid in all cases of syphilis was begun. Previous to this time important contributions suggesting the frequency of involvement of the nervous system in early syphilis had already appeared in the literature in France by Ravaut,¹ in Germany by Altman and Dreyfus,² and in this country by Engman³ and his co-workers. In 1914 and 1915 studies from this clinic appeared on the involvement of the nervous system, particularly in reference to the secondary period of the disease, by Wile and Stokes.⁴ The results of these studies showed that the invasion of the nervous system occurred extremely early, that it was frequently seriously involved without symptoms, and that serious involvement might escape detection unless the routine lumbar puncture was practiced on all cases. The high percentage of involvement in early syphilis led us at that time to state our belief that "the fate of every syphilitic with regard to the incidence of cerebrospinal lues, whether this occurs early or late in the course of the disease, is determined in the first months of the infection." Our results in the main have been confirmed by the contemporary writers and subsequent publications.

1. Ravaut: *Ann. de dermat. et syph.*, Ser. 4, No. 2: 1 and 537; 1903; Ser. 4, No. 5: 1057, 1904; Ser. 4, No. 8: 1057, 1907; *Rev. mens. d. méd. inst.*, No. 3: 1, 1909.

2. Altman and Dreyfus: *München. med. Wchnschr.* **5**:465, 1913. Dreyfus: *München. med. Wchnschr.* **59**:2567, 1912.

3. Engman, M. F.; Buhman, R.; Gorham, F. D., and Davis, R. H.: *A Study of the Spinal Fluid in One Hundred Cases of Syphilis*, *J. A. M. A.* **61**:735 (Sept. 6) 1913.

4. Wile and Stokes: *A Study of the Spinal Fluid with Reference to Involvement of the Nervous System in Secondary Syphilis*, *Dermat. Wchnschr.* **59**:1079, 1107 and 1128, 1914.

At present we have at our disposal, for the purpose of study, 1,869 cases of syphilis in all stages, on which routine lumbar punctures have been carried out, together with careful study of the associated findings. This number represents about one third of the total number of cases of syphilis seen during this period.

The cases included in this group have been selected particularly with reference to correct diagnosis, and the number is limited to those that have been accurately observed over a definite period of time. Cases of doubtful diagnosis and cases seen casually have been cast aside.

TYPES OF SYPHILIS STUDIED

According to the clinical findings, the cases have been divided into the following types: congenital syphilis, primary syphilis (chancre only present), secondary syphilis, late syphilis of the skin and mucous membranes (tertiary), latent syphilis, tabes, general paresis, taboparesis and diffuse cerebrospinal syphilis. In Table 1 will be found the number of cases in each group.

TABLE 1.—CLASSIFIED TYPES OF CASES

Type of Syphilitic Involvement	Number of Cases
Congenital.....	53
Primary.....	236
Secondary.....	508
Tertiary.....	155
Latent.....	568
Diffuse cerebrospinal.....	178
Tabes dorsalis.....	109
General paresis.....	49
Taboparesis.....	13

TABLE 2.—NUMBER OF CASES WITH PLEOCYTOSIS AS FOUND IN VARIOUS TYPES OF SYPHILIS STUDIED, WITH THE PERCENTAGE INVOLVEMENT

Type of Syphilitic Involvement	Number of Cases	Number With Increased Cells	Percentage With Increased Cells
Congenital.....	53	14	26.4
Primary.....	236	38	16.1
Secondary.....	508	173	34.0
Tertiary.....	155	39	25.1
Latent.....	568	163	28.6
Diffuse cerebrospinal.....	178	157	88.2
Tabes dorsalis.....	109	102	93.5
General paresis.....	49	47	95.9
Taboparesis.....	13	13	100.0

The ordinary criteria, as now accepted, indicating the involvement of the nervous system are the standards used in this study. Thus, a cell count of over 6, the presence of increased albumin and globulin and the Wassermann test on the spinal fluid are considered, as well as the Lange gold curve in a certain number of selected cases.

In order to determine the parallelism, if any exists, between the various criteria, separate tables are given. Table 2 shows the percentage of involvement as indicated by increased cell count. Table 3 indicates the percentage of involvement as shown by increased globulin and albumin content in the fluid. Table 4 shows the percentage of involvement as indicated by the positive Wassermann test on the fluid.

TABLE 3.—NUMBER OF CASES WITH INCREASED ORGANIC SOLIDS AND THE PERCENTAGE OF INCREASE IN THE VARIOUS TYPES STUDIED

Type of Syphilitic Involvement	Number of Cases	Number With Increased Albumin and Globulin	Percentage With Increased Albumin and Globulin
Congenital.....	53	7	13.2
Primary.....	236	45	19.0
Secondary.....	508	178	35.1
Tertiary.....	155	41	26.4
Latent.....	568	154	27.1
Diffuse cerebrospinal.....	178	173	97.2
Tabes dorsalis.....	109	107	98.1
General paresis.....	49	47	95.9
Taboparesis.....	13	13	100.0

TABLE 4.—NUMBER OF CASES WITH A POSITIVE WASSERMANN REACTION OF THE SPINAL FLUID AND THE PERCENTAGE WITH POSITIVE REACTIONS IN THE VARIOUS TYPES STUDIED

Type of Syphilitic Involvement	Number of Cases	Number With Positive Wassermann Reaction	Percentage With Positive Wassermann Reaction
Congenital.....	53	9	16.9
Primary.....	236	14	5.9
Secondary.....	508	135	26.5
Tertiary.....	155	48	30.9
Latent.....	568	159	27.9
Diffuse cerebrospinal.....	178	156	87.6
Tabes dorsalis.....	109	102	93.5
General paresis.....	49	47	95.9
Taboparesis.....	13	13	100.0

From a study of these tables it will be seen that in each group of cases a fair degree of parallelism exists in the ratio of involvement, as shown by each of the criteria. In the main, the increase in globulin is found slightly more frequently than any other single finding, and this increase was almost constantly parallel with an increase in the number of cells present. A slightly lower percentage of involvement is seen in the column of Wassermann tests.

From the standpoint of delicacy of all tests, general paresis and taboparesis yield the highest percentage, 100 per cent being found positive in all columns in the combined type and 95 per cent. in all columns in the straight, frank paresis. Tabes is slightly lower and the diffuse form of cerebrospinal syphilis ranks last in the uniformity of positive criteria, although still showing a high percentage of parallelism with the clinical findings.

The material included in this study presents many interesting points of discussion, each one of which might well be the subject of a separate paper. It is expected that these will so be treated in the near future. In this particular study we wish to emphasize three distinct interesting points that have been brought out in our analysis of the cases. First: The strikingly high percentage of neurosyphilis associated with syphilitic alopecia, iritis and leukoderma colli. Second: The association of neurosyphilis with late syphilids of the skin, bones and viscera. Third: The high percentage of asymptomatic neurosyphilis occurring during the indefinite period of latency.

NEUROSYPHILIS ASSOCIATED WITH SYPHILITIC ALOPECIA, IRITIS AND LEUKODERMA

Early in our study we were struck by the great frequency with which neurosyphilis, particularly as indicated by practically all criteria in the spinal fluid, was associated with syphilitic alopecia. From our cases of this complication we find that of forty-six cases showing this symptom, 73 per cent. had coincident involvement of the nervous system. Practically all cases in which involvement occurred were characterized by a considerable degree of pleocytosis. A few patients had symptoms of headache; none had distinct organic signs, except such indefinite ones as increased reflexes. Many with a high degree of involvement were absolutely without symptoms.

Alopecia as a complication occurred in about 6 per cent. of all of our secondary cases. The mechanism of specific alopecia is not clearly understood, and we suggest that this mechanism may actually relate, at least in some cases, back to a disorder of enervation, being associated with the coincident cerebrospinal involvement, rather than due to a direct involvement of the hair follicle by spirochetes.

A similarly interesting and uniformly high association was found in the complication of secondary iritis. In our series this occurred in twenty-one of 508 secondary cases of syphilis studied. Associated cerebrospinal involvement occurred in fifteen of these twenty-one cases, or 71.4 per cent.

Of the more tardy secondary syphilids, a high percentage of involvement of the nervous system was found in association with leukoderma colli. Our figures of this manifestation are rather small, only eleven cases having been seen. Of this number, however, 55 per cent. were found distinctly positive in the spinal fluid.

NEUROSYPHILIS AND SYPHILIS OF THE SKIN, BONES AND VISCERA

We may turn now to the association of the central nervous involvement with other forms of late syphilis, particularly those of the skin, bones and viscera. It is a common teaching and a general belief that

an inverse ratio exists between cerebrospinal involvement and other forms of late syphilis. For example, it is believed that tabetics and parietic patients and patients with other cases of late neurosyphilis with outstanding symptoms are seldom seen with late manifestations in the splanchnic system or in the skin and bones. This belief is at least held by some to be clinical evidence suggesting the existence of spirochete neurotropism. Whatever the merits of the question of spirochete strains are, and certainly considerable evidence exists tending to substantiate their existence, we are convinced from our study that this question cannot find a reliable argument in the lack of coincidence of late neurosyphilis and other forms of gummatous involvement. Thus, we find that in 155 cases of late syphilis involving the skin and mucous membranes, the bones and the viscera in the form of gummas and diffuse syphilomas, forty-eight cases, or 30 per cent., showed involvement of the nervous system at the same time. We found a frequent association, for example, of tabes and hepatic syphilis and aortitis, and in a few cases, of paresis and tabes with definite gummatous lesions in the skin.

The predominance of the neurologic symptoms and signs in cases of late syphilis of the nervous system and the fact that many of these cases are studied merely from the angle either of their psychiatric or neurologic aspects has undoubtedly led to the failure to recognize coexistent visceropathies.

Our studies have for the most part been made when patients showed definite involvement of the viscera, the skin or bones and when on examination we have been able to demonstrate the coincident cerebrospinal disease. From an experience extending over eight years, during which time we have had occasion to examine cases of late cerebrospinal syphilis in all forms referred to us from other services, we have been similarly struck with fully as high a percentage of associated splanchnic, cutaneous and osseous syphilis when the cases are viewed from this angle.

NEUROSYPHILIS OCCURRING DURING PERIOD OF LATENCY

Studying our figures from the standpoint of the occurrence of cerebrospinal involvement with asymptomatic syphilis, we find that in the latent period of the disease about 28 per cent. of all patients showed distinct involvement, as shown by increased cell count, increased organic solids and the Wassermann reaction in the fluid. This group of cases is made up largely of patients who have consulted the hospital for reexamination as to a preexisting syphilis. A large part of this group, however, is composed of those who had entered the hospital for some other complaint and who had been referred to this department:

on the basis of the positive Wassermann blood test. In this group, entirely asymptomatic from the standpoint of the nervous system as well as from the general constitutional manifestations, we found, studying these patients from the standpoint of the colloidal gold curve, that a number gave typical paretic curves, others the curve of tabes.

To state with any degree of definiteness that these asymptomatic patients would inevitably develop active manifestations is perhaps too dogmatic in the light of our present knowledge. Such cases, however, in which the existence of cerebrospinal involvement is unknown to the patient and makes itself known only through the lumbar puncture, findings are extremely important when viewed from the standpoint of the patient, the community and, in general, the prognosis of the disease. We believe that if these patients had been examined early in the course of the disease the involvement would have been demonstrated at that time and if through intensive treatment it had been directed to the nervous system, the patient might have been saved the later complication. In that particular type of case in which an acute meningeal reaction occurs early, with or without symptoms, we have been impressed with the rapidity with which the fluid can be restored to normal through intensive constitutional and intraspinal medication.

That some patients of this group, asymptomatic at the time of puncture, actually did develop symptomatic neurosyphilis, we were able to demonstrate in a few of the cases under observation for several years. Thus, for example, we have seen definite paretic symptoms develop in a few cases in which at the preliminary puncture the paresis was manifested only by the Lange gold curve.

CONCLUSIONS

1. The nervous system, if uninvolved as shown by the accepted criteria during the first months of the infection, is seldom invaded later. A negative preliminary puncture followed by positive findings at a later date occurred in only three of several thousand cases punctured.

2. Of the several criteria indicating involvement, the increase of organic solids is found to be slightly higher than either the cell count or the Wassermann reaction, the relative value being indicated in the order just mentioned.

3. A considerable degree of cerebrospinal involvement may be present in the latent period of syphilis without manifesting any signs or symptoms.

4. Such asymptomatic cases may become symptomatic later, and a study of the colloidal gold curve in these cases is of some value in estimating the ultimate prognosis of the case.

5. Comparing the large number of cases of primary and secondary syphilis in which positive findings are found, with the relatively small percentage of late neurosyphilis as compared to total syphilitic incidence, we must conclude that a large number of early cases are in the nature of a meningeal roseola, which is transitory in its clinical aspects.

6. The interpretation of the lumbar puncture findings, particularly early in the incidence of the disease, constitutes a valuable guide in estimating the ultimate prognosis of the disease with regard to the integrity of the nervous system.⁵

5. In addition to the references already given, the following may be of interest:

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Widal and Ravaut: *Soc. med. d. hôp.*, June, 1905.

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Fildes, P.; Parnell, R. J. G., and Maitland, H. B.: *Unsuspected Involvement of the Central Nervous System in Syphilis*, *Arch. Neurol. & Psychiat.* **1**:231 (Feb.) 1919.

Sutter: *New York J. M.* **17**:23, 1917.

Keyser: *Cleveland M. J.* **16**:337, 1917.

With: *Brain* **40**:403, 1917.

Fordyce, J. A.: *Med. Rec.* **91**:927, 1917; *Neurosyphilis*, *J. A. M. A.* **71**:1023 (Sept. 28) 1918; *Am. J. Syphilis* **3**:337, 1919.

Larkin and Cornwall: *Am. J. Syphilis* **3**:76 (Jan.) 1919.

Scott and Pearson: *Am. J. Syphilis* **21**:201, 1920.

Ellis and Swift: *J. Exper. Med.* **18**:162, 1913.

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Sicard and Roger: *Presse méd.* **26**:457, 1918.

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AN ATTEMPT TO IMPROVE THE SENSITIVENESS OF THE COMPLEMENT-FIXATION TEST FOR SYPHILIS WITHOUT LOSS OF ACCURACY

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It is a well-known fact that varying amounts of the antilipoidal substances of syphilitic serum which are responsible for the fixation of complement in the Wassermann reaction are lost in the process of inactivation. This accounts in part for the higher percentage of positive reactions obtained by some of the raw serum methods, as compared with the classic Wassermann test. That there is a general desire for a more sensitive test is indicated by the numerous complement-fixation tests with noninactivated serum that have been employed. There is, however, a prevailing distrust of raw serum methods for routine diagnosis on account of the risk of false positive reactions—and not without reason. If a test can be devised that will be as free from the possibility of false positive reactions as is the Wassermann test and at the same time be as delicate as the better known raw serum tests, such as the Noguchi and Gradwohl, it will fill a real need. I shall describe a test that I believe has this degree of safety with the advantage of greater delicacy.

RELATIVE MERITS OF GUINEA-PIG AND HUMAN COMPLEMENT

In a reliable raw serum test the native complement present must be taken into account and used to best advantage. As having a bearing on one of the claims of superiority of such a test, the relative merits of guinea-pig and human complement is the first subject for consideration.

The most important advantage of human complement is its greater fixability by antigen-antibody combination as compared with that of guinea-pig serum. This property of human complement plus the larger quantity of antibody in noninactivated serum yields positive reactions that would escape a heated serum and guinea-pig complement method, and converts weak reactions into strong ones.

The second advantage of human complement is that, being a normal constituent of human serum, it is not subject to serious anticomplementary action on the part of the patient's serum. Means for eliminating this difficulty entirely are provided for in the test to be described.

Guinea-pigs can be dispensed with entirely if human serum is used.

As to the disadvantages: Human complement is said to be more susceptible to nonspecific fixation by antigen plus serum than is guinea-pig complement; it therefore follows that means must be provided in a satisfactory raw serum test to guard against the occurrence of falsely positive results from this cause. In tests utilizing only the complement of the serum to be tested, the precaution of titration with antigen cannot be carried out as it is impossible even with a testing of each serum to titrate the complement in a positive serum in the presence of antigen.

Lack of fixability, but with full lytic activity, occurs occasionally with the complements of individual persons and also of guinea-pigs, resulting in false negative reactions. This is one of the drawbacks of a system employing the natural complement of the serum tested, and accounts for the occasional false negative results in raw serum systems that should theoretically reveal the smallest traces of syphilitic amboceptor. False negatives of this kind occur with tests like the newer Noguchi, Gradwohl, Thompson, and, in fact, with practically all of the raw serum methods and with all others using complement from a single animal.

The next consideration is the hemolytic system. Human and sheep cells are used almost exclusively and, for various reasons, principally of convenience, doubtless will continue to be used to the practical exclusion of others. According to Kolmer, Matsunami and Rule,¹ the antihuman hemolytic system is somewhat more sensitive than the anti-sheep, but this is more pronounced in high dilutions of positive serums than in the usual quantities. This slight advantage, and also whatever advantage may reside in the greater availability of human blood, is more than counterbalanced by the difficulty of obtaining a high titer antihuman rabbit serum and the annoyance of the presence of agglutinins for human cells both in the rabbit serum and in the test serum. These agglutinins are probably partly responsible for the false positive reactions obtainable occasionally with the Noguchi test. Where it is necessary to fortify the complement content of the serum by the addition of fresh negative serum, the difficulty is increased proportionately.

ADJUSTMENT OF REAGENTS

Means for the reasonably accurate adjustment of the factors of the hemolytic system are essential to a reliable test. It is true that such tests as the Hecht-Gradwohl, in which both native complement and

1. Kolmer, J. A.; Matsunami, T., and Rule, A.: Standardization of the Wassermann Reaction, A Comparative Study of Complement Fixation in Syphilis with Antihuman, Antichicken and Antisheep Hemolytic Systems, *Am. J. Syph.* **4**:278 (April) 1920.

native amboceptor are utilized, are quite accurate, for although the ratio between complement and amboceptor are unknown, the practical equivalent is obtained in the finding of the hemolytic unit. Theoretically, if the test serum should be strong in hemolysin, the lytic unit would contain such a small amount of complement as to be absorbed nonspecifically, thus giving false positive reactions.

The adjustment of the hemolytic system is of great importance, not only in regard to the balance between complement and amboceptor, but also between the size of the unit of these reagents in relation to the volume of test serum employed. If the complement is titrated against a fixed amount of amboceptor and this amount is unduly large, the unit of complement may be so small as to be absorbed nonspecifically. On the other hand, if the unit of complement is too large, a positive serum may be unable to fix the whole amount, thus causing a weaker reaction than would have been obtained with the proper adjustment. If the amount of patients' serum is too small in proportion to the other ingredients, delicacy of reaction is lost by inability of a weak serum to absorb all the complement. If the amount of patients' serum is too large in proportion to the elements of the hemolytic system, false positives may result from loss of complement through partial nonspecific fixation by the serum-antigen mixture. An excess of amboceptor may be present in those methods in which an antish sheep system is used without taking into account the native amboceptor in the patients' serum. The methods of Stern and of Hecht and the original Wassermann test are subject to this criticism. Excess of amboceptor is capable of dissociating complement and thus rendering tests less delicate. Seelman² has devised a raw serum method in which the amount of complement and native amboceptor are both estimated in an ingenious manner, but it is too complicated for the rank and file of serologists. It should, however, be fairly safe against false positives since the adjustment of the hemolytic system is such that foreign complement has frequently to be added.

While it is desirable that a system should have as few false negative reactions as possible, it is more important that it should not be subject to the danger of false positive reactions. The present system, while capable of giving a very small percentage of false negative reactions as is true of other human complement methods, has an advantage over those in which noninactivated serum with complement from a single individual is used—such as the Noguchi and others depending on the use of very fresh serum—the adjustment of the hemolytic system being such as to avoid the necessity of adding any foreign complement. This point will be more fully brought out in the description of the technic.

2. Seelman, J. J.: A Raw Serum Wassermann Test Employing the Sheep Hemolytic System, *Am. J. Syph.* **4**:157 (Jan.) 1920.

TECHNIC OF THE PROPOSED METHOD

Hemolytic System.—Sheep's blood is washed three times and the measure made up to the original volume of the blood. For use in the test and in titrating reagents it is diluted five times, making a 20 per cent suspension.

Amboceptor.—This is made up of rabbit antisheep immune serum standardized by titration of varying dilutions in amounts of 0.2 c.c. against 0.2 c.c. of 20 per cent. guinea-pig serum, pooled from several pigs, and from two to four hours old on the clot, and 0.2 c.c. of 20 per cent. suspension of sheeps' blood with salt solution to make 2.0 c.c.

Complement.—This is composed of human serum, pooled from the negative serums of the previous days' tests and titrated against the unit of amboceptor before each test, or guinea-pig serum pooled from several pigs and titrated in the same manner. If human serum is used, it must be de-amboceptorized, as described later. In either case, the unit of complement is 0.2 c.c. of the weakest dilution just giving complete hemolysis of 0.2 c.c. of 20 per cent. blood with one unit of amboceptor in 10 minutes.

Antigen.—The antigen used is Noguchi's acetone insoluble. It is advisable to standardize the antigen with human complement if the latter is to be used, and to prepare dilutions for the test containing five antigenic units in 0.2 c.c., the amount used in the test.

Patients' Serum.—Five-tenths c.c. of the serum to be tested is placed in a tube and 0.5 c.c. of a 33 per cent. suspension of whole sheep's blood is added. The tubes are immediately placed in cracked ice. Melting ice has a temperature of 1 C., at which point the amboceptor is fixed, but not complement, and no hemolysis takes place. After standing one hour in the ice, the tubes are centrifuged and the clear serum pipetted off into the tubes for the test.

The process of removing the natural amboceptor from the serum in a laboratory properly equipped with a high speed centrifuge is no trouble whatever. The tubes are placed, three or four in each of the eight holders. (Most machines are equipped with an eight place head.) A few seconds after the motor has reached full speed, the current is shut off and it will be found that the cells are packed in the bottom of the tubes, which are returned to the ice water until pipetted off into the tubes for the test. Most of the time required for this process is consumed in pipetting off the serums from the clots, and adding the sheep cells. The time required in weighing up the tubes, placing in the machine, whirling and then removing is not more than twenty minutes for fifty specimens.

Preliminary Titration.—As before stated, the value of the antisheep amboceptor is established in the beginning, and thereafter a fixed quan-

tity is used for titrating complement and in the test. If guinea-pig complement is to be used, dilutions of 1 to 5, 1 to 6, 1 to 8, and 1 to 10 are made up as follows:

TABLE 1.—GUINEA-PIG COMPLEMENT

Guinea-Pig Serum, C.c.	Salt Solution, C.c.	Dilution
0.1	0.4	1 to 5
0.1	0.5	1 to 6
0.1	0.7	1 to 8
0.1	0.9	1 to 10
0.1	1.1	1 to 12

A row of five tubes is set up and in each is placed one of the complement dilutions, 0.2 c.c., amboceptor dilution of the titer strength, 0.2 c.c. (1 unit), sheep's blood (20 per cent), 0.2 c.c., and salt solution 1.4 c.c.

If human serum is used for complement, it is first de-amboceptorized by adding one part of whole blood to three parts of serum, chilling and centrifuging as already described. In its titration, four tubes are set up containing, respectively, 0.2, 0.15, 0.1 and 0.05 c.c. of the serum; otherwise the process is the same as for guinea-pig serum. The smallest amount causing complete hemolysis in ten minutes has the value of one unit.

Setting Up the Test.—Three tubes only are required for the test. In addition to the test serums, a positive control should be set up. The back tube is for the purpose of estimating the amount of complement present in the serum and for the anticomplementary control. The two front tubes are for the test proper. Into each of the three tubes is placed 0.2 c.c. of the de-amboceptorized patient's serum, which contains 0.1 c.c. of undiluted serum. The front and middle tubes receive in addition 0.2 c.c. of antigen and 1.0 c.c. of salt solution, and the front tube receives one-half unit of complement. The back tube receives, besides the serum, 0.2 c.c. of amboceptor dilution of such strength that it contains one and one half units, 0.2 c.c. of sheep cells, (20 per cent. blood) and 1.4 c.c. of salt solution. The tubes are placed in the 37 degrees bath for preliminary fixation of whatever complement may be present in the first two tubes, and to estimate the amount of complement present by the rate of hemolysis in the back tube. This can be gaged closely as the exact amount of amboceptor is known. On the rate of hemolysis depends the decision of how much complement to add to the front and middle tubes. The plan is to have one half unit of complement in the front tube in excess of the amount in the middle tube. The object of this is, first, to facilitate the reading of

results: Since the strength of reaction is a measure of the fixing power of antibody-antigen, it follows that strongly positive serums will bind all the complement in both tubes, whereas a weaker one may fix the complement in the middle tube but not all in the front tube. The reading of results is, therefore, much easier as well as more accurate than when one tube only is used, but the most important function of the excess of complement in the front tube is to introduce a pooled complement into the test, thereby guarding against the chance of false positive reactions.

TABLE 2.—COMPLEMENT FIXATION TEST

First incubation, 10 minutes					
Front Tube		Middle Tube		Back Tube	
Serum	0.2 c.c.	Serum	0.2 c.c.	Serum	0.2 c.c.
Complement, $\frac{1}{2}$ unit				Amboceptor	0.2 c.c.
Antigen	0.2 c.c.	Antigen	0.2 c.c.	Sheep cells.....	0.2 c.c.
Salt solution.....	1.0 c.c.	Salt solution.....	1.0 c.c.	Salt solution....	1.4 c.c.
Continuation of first incubation, 20 minutes					
Comp. q. s.		Comp. q. s.		Comp. q. s.	
Second incubation, 15 minutes					
Amboceptor	0.2 c.c.	Amboceptor	0.2 c.c.	Amboceptor	0.2 c.c.
Sheep cells.....	0.2 c.c.	Sheep cells.....	0.2 c.c.	Sheep cells.....	0.2 c.c.

Individual complements sometimes possess the peculiar property of nonspecific absorption by antigen plus serum, the control tube without antigen clearing up. In this event the extra foreign complement in the front tube causes complete hemolysis, and no mistake occurs. Having placed the tube racks in the water bath, the rear tubes should be inspected at frequent intervals. If hemolysis occurs in four minutes, in the presence of $1\frac{1}{2}$ units of amboceptor, it indicates the presence of one unit of complement; hemolysis in from six to seven minutes means one half unit and in from twelve to fourteen minutes, one fourth unit. At the end of ten minutes, one fourth unit of complement is added to all three tubes of those sets in which hemolysis is not quite complete in the back tube and one half unit to those sets in which hemolysis is slight. Any tubes not completely hemolyzed in another ten minutes are anticomplementary and another half unit should be added. In the case of persistently anticomplementary serums, this should be repeated at intervals of ten minutes until hemolysis is complete. Anticomplementary results are thus eliminated entirely. Incubation is continued for twenty minutes after the last addition of complement and blood, 0.2 c.c., and amboceptor, $1\frac{1}{2}$ units, are added to the first two tubes. The results are read fifteen minutes after the addition of cells and amboceptor.

Reading of Results.—Complete inhibition in the second tube is a definite or +++ positive reaction, provided inhibition is marked in the first tube.

Complete hemolysis in the first tube should cause one to regard with suspicion any inhibition in the second tube as possibly being due to nonspecific fixation. If, under these circumstances (complete hemolysis in the first tube), the hemolysis is only partial in the second tube, the result may be accepted and recorded as + or ++, as the case may be. If, however, there is no hemolysis in the second tube and complete hemolysis in the first tube, the safest plan is to reject the result entirely.

Almost complete inhibition in the second tube, with a varying degree, but less, in the first tube, is a ++ reaction.

A + reaction, as before stated, is recorded when the inhibition in the second tube is slight but definite.

The control tubes must, of course, be clear in all cases.

ADVANTAGES CLAIMED FOR THE METHOD

1. It is a raw serum method, consequently more delicate than is possible for an inactivated serum method.

2. The amounts of both complement and amboceptor are known and controlled.

3. False negatives from an insufficient amount of complement are impossible.

4. The method is applicable to all serums, regardless of age or the amount of complement contained, and to spinal fluids.

5. It is as simple and no more time consuming than the regular Wassermann test.

6. False positive reactions, which are due to nonspecific fixation either from too small an amount of complement or on account of peculiar properties of individual complements, are impossible because of the use of two antigen tubes, one of which contains pooled complements in excess of hemolytic requirements. The use of acetone insoluble antigen removes the last vestige of chance for false positive reactions.

7. No anticomplementary results are obtained.

THE SACHS-GEORGI REACTION FOR SYPHILIS

A PRELIMINARY REPORT OF MORE THAN ONE THOUSAND COMPARATIVE WASSERMANN AND SACHS-GEORGI TESTS *

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The Wassermann reaction for syphilis, despite its wide clinical acceptance, cannot be regarded as free from certain inherent defects. The mere fact that the test requires a considerable number of biologic reagents for its performance, all of which are to some degree variable and uncertain, is perhaps one of the reasons that the results of the test are not always reliable even when in the hands of the conscientious worker. We must furthermore recognize that a definite number of cases clinically positive are serologically negative. The standardization of the biologic reagents might seem a logical improvement, and efforts are being made in this direction by the German authorities. Efforts to simplify the technic have repeatedly been made, particularly since the recognition that the reaction is essentially physicochemical, not depending on specific immunologic alterations in the serum of the syphilitic. Perhaps the flocculation reactions, such as those described by Porges and Meyer, Herman-Perutz, Bruck, Klausner and others, gave evidence of progress in this direction, although none of them offered a real substitute for the Wassermann test.

The increased use of tests for syphilis, as well as the general shortage of the necessary biologic reagents incident to the war, made a reinvestigation of the problem desirable. Two tests have been developed: that of Meinicke,¹ and that of Sachs-Georgi,² which are evidently of considerable usefulness. Of these, the Sachs-Georgi, because of its remarkable simplicity as well as its seeming specificity, has found most favor. The obvious importance of simplified serologic procedure would warrant a careful comparison of such tests with the Wassermann reaction, and we have therefore examined over one thousand serums and spinal fluids by the Sachs-Georgi technic.

TECHNIC

The technic of the Sachs-Georgi test which we have employed is the modification proposed by Mandelbaum,³ which differs from the

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1. Meinicke, E.: *Berl. klin. Wchnschr.*, **55**:83, 1918.

2. Sachs, H., and Georgi, W.: *Med. Klin.* **14**:610, 1918.

3. Mandelbaum, M.: *München. med. Wchnschr.* **65**:294, 1918.

original in the use of smaller amounts of serum and antigen. The serum or spinal fluid to be tested must be absolutely clear after being centrifuged, free from cotton fibers or other particles. It is inactivated in the water bath at 56 C. for one half hour. Three drops of serum are then mixed with 1 c.c. of sterile salt solution (0.85 per cent.). To this diluted serum, 0.5 c.c. of cholesterinized alcoholic beef heart antigen, which has been previously diluted 1 to 6 with 0.85 per cent. salt solution, is added. The tubes are then gently agitated and placed in the incubator at 37 C. for from eighteen to twenty-four hours. A reading is taken at this time; most of the positive serums will have flocculated. The tubes are kept at room temperature for the next twenty-four hours, and final readings are then made.

Apparatus.—Glassware must be perfectly clean. We have our tubes washed in tap water, then placed in an acid cleaning bath for several hours, washed in tap water and finally rinsed several times in distilled water. They are then dried in the hot air oven. Sterile pipets are used.

Serum.—The question that has been raised in the Wassermann technic concerning the use of active or inactive serum is also involved in the Sachs-Georgi test. Mandelbaum dilutes the fresh serum and then inactivates it before adding the antigen. We have used the inactivated serum, then diluted and added the antigen. Other observers prefer to keep the serum on ice several hours before inactivating, assuming that because of certain alterations brought about by the chilling of the seroglobulins, the reaction is made more sensitive.

Diluting Agents.—In the Wassermann reaction, approximate isotonicity seems sufficient, minor variations in the concentration of the salt being without effect on the reaction. In the Sachs-Georgi reaction we have found that reliable results can be obtained only when the salt solution is made up to 0.85 per cent. The salt solution should, of course, be sterilized.

Antigens.—The preparation of the proper antigen is perhaps the fundamental factor in the success or failure of the Sachs-Georgi reaction. Extracts from human, beef, pig, guinea-pig and sheep heart have been used, as well as from beef and syphilitic fetal liver. Our most satisfactory results have been obtained with an antigen thus prepared: Beef heart cut into small pieces was ground in a meat grinder; 5 c.c. of alcohol (95 per cent.) per gram of moist heart substance was then poured over the mass and incubated at 37 C. for from eight to ten days. During this time the flask was shaken each day. The alcoholic extract was then filtered and cholesterinized. The amount of cholesterin needed varies with each antigen. We have found it good practice to titrate the antigen against positive and neg-

ative serums after adding various dilutions of cholesterin to small fractions of the antigen and selecting the proper amount of cholesterin to be added according to our actual serum titration. Sachs and Georgi thus prepared their antigen: To 100 c.c. of filtered beef heart extract and 200 c.c. of alcohol is added 13.5 c.c. of a 1 per cent. alcoholic solution of cholesterin.

Before use the antigen is diluted 1:6 with salt solution. The dilution must be made neither too slowly nor too rapidly. The extract when properly made is quite clear, the diluted antigen faintly opalescent and does not flocculate after standing several days. The antigen when diluted 1:10 serves very well as an antigen for the Wassermann reaction.

Incubation.—In the original Sachs-Georgi technic, the tubes were incubated for two hours and then placed at room temperature for twenty-four hours. Mandelbaum, Hauck,⁴ Ammenshauser⁵ and others have shown that better results are obtained if the incubation is prolonged for from eighteen to twenty-four hours. The tubes are then read and kept at room temperature for another twenty-four hours before the final reading is made. Sachs and Georgi have adopted this modification.

Reading of Results.—Most of the German workers have used the agglutinoscope devised by Kuhn and Voit to read the results. A good magnifying lens from a dissecting microscope or even the ocular from a microscope can, however, be used with very satisfactory results if the tubes are held against a dark background. The flocculation may be very fine—smoky, finely granular—driven snow, or may finally be precipitated at the bottom of the tube as a coarsely granular floccular mass. Gentle rotation or agitation of the tube aids observation. Negative cases remain perfectly clear for twenty-four hours, later a slight precipitate may collect at the bottom of the tube, but this can readily be differentiated from positive findings. In a general way, one can grade the degree of the reaction on a one to four plus basis; in a few cases we have recorded plus-minus readings. With the use of the agglutinoscope, the number of doubtful readings would probably be increased. We have found it useful to centrifuge doubtful tubes at low speed for half an hour and then pour off some of the supernatant fluid. By comparison with negative tubes similarly treated, minor differences become more apparent. We have also kept the tubes on ice after incubation, but have found no superiority over simple room temperature from this procedure.

4. Hauck, L.: Influence of Temperature on Sachs-Georgi Reaction, München. med. Wchnschr. **67**:369 (March 26) 1920.

5. Ammenshauser: Centralbl. f. Bakteriöl., **84**:521, 1920.

RESULTS OF EXAMINATION

In Table 1 are recorded the results of 1,042 examinations made with the Wassermann and the Sachs-Georgi tests. The serums and cerebrospinal fluids were obtained from the serologists of the Cook County Hospital and the city board of health; their Wassermann reports were based on tests with from two to four antigens.

TABLE 1.—RESULTS WITH WASSERMANN AND SACHS-GEORGI TESTS

Reaction	Result								
	Positive			Negative			Anticomplementary		
Wassermann.....	+	±	—	+	±	—	+	±	—
Sachs-Georgi.....	163	5	3	44	9	634	2	0	3
Total.....	866								

In Table 1 it will be observed that in 163 cases there was an agreement of positive cases (18.8 per cent.) and in 634 an agreement of negative cases (73.2 per cent.), i. e., an agreement of 92 per cent.

The results with cerebrospinal fluids are given in Table 2

TABLE 2.—RESULTS WITH CEREBROSPINAL FLUID

Reaction	Result								
	Positive			Negative			Anticomplementary		
Wassermann.....	+	±	—	+	±	—	+	±	—
Sachs-Georgi.....	36	6	3	7	2	121	1	0	0
Total.....	176								

The total agreement in this series was 157, or 89.2 per cent.

Of the total number of serums and cerebrospinal fluids examined (1,042), sixty-two were found to give a positive or plus-minus Sachs-Georgi reaction while the Wassermann was negative. The details in our possession concerning these cases are recorded in Table 3

It will be observed that the clinical history or the physical findings in thirty-six of these patients made a diagnosis of syphilis probable (58 per cent.). In twenty, the reaction seems nonspecific (32 per cent.), while in six cases we have no information that would assist in the determination of the correctness of the serologic finding.

From a summary of 17,186 serum tests reported by a number of observers and collected by Baumgärtel ⁶ (to which are added the 7,000 reported by him), Table 4 has been constructed.

It will be observed that in 5,808 positive cases and in 15,950 negative cases, there was complete agreement, as well as in 246 doubtful reactions, 91 per cent. of the total. Of the discrepancies (9 per cent.),

6. Baumgärtel, T.: Parallel Wassermann and Sachs-Georgi Tests, München. med. Wchnschr. 67:421 (April 9) 1920.

TABLE 3.—CLINICAL CORRELATION OF CASES WITH POSITIVE SACHS-GEORGI REACTION AND NEGATIVE WASSERMANN REACTION

No. of Patient	Clinical Diagnosis on Admission	Clinical History	Treatment
xi-16	Suspected syphilis	Gonorrhea twice; chancre two months ago; now in second stage	None
ix-3	Chancroid	Primary syphilis; inguinal and epitrochlear glands enlarged; ulcer of scrotum	None
ix-32-34	Cerebral hemorrhage	History of chancre; rigid, irregular pupils; spinal fluid examination: pressure + + +, globulins + +, 88 lymphocytes	None
ix-33	Cerebral hemorrhage	Paralysis, left leg; patellar reflexes, + + +; absent abdominal and cremasteric reflexes	Potassium iodid and mercury
viii-12	Acute arthritis	History of transient attacks of paraplegia; roentgen-ray, hypertrophic osteoarthritis; denies syphilitic infection	Improved under potassium iodid
viii-26	Chronic nephritis and endocarditis	Gonorrhea once, denies syphilis; pupils sluggish to light; absent patellar and cremasteric reflexes; shuffling gait; wife one miscarriage	None
vii-37	Bronchopneumonia and syphilis	Gonorrhea and buboes; punched-out scar on prepuce; slight adenopathy; epitrochlear glands	Intravenous medication 11/9/20 N. W. U. Post-Grad. M. Sch.
vii-64	General paresis	History of chancre and secondary syphilis; gastric crisis; tabetic gait and urinary incontinence; loss of memory	None
vi-8	General paresis	Chancre fourteen years ago; syphilitic erosion of nose; incontinence of urine; difficulty in walking at night; gastric crisis; patellar reflex, + +; Romberg sign, + +; Argyll Robertson pupils and scanning speech	Now on syphilitic treatment
vi-11-52	Syphilitic thrombosis	Chancre fifteen years ago; hemiplegia; amnesia; pupils sluggish; eyelids drooping; spinal fluid examination: pressure + +, globulin +, 16 cells	Has had six injections of arsphenamin
vi-24	Syphilitic epiphysitis	Congenital syphilis; palmar and plantar desquamation; rhagades about mouth; suggestive syphilitic nose	None
vi-51	Crossed paralysis of sixth and seventh cranial nerves	Chancre two years ago; paralysis, right side of face; secondaries, hands and face; spastic and ataxic gait; Romberg, + + +; patellar, + + +; spinal fluid examination: pressure + +, globulins + +; 12 cells	None
v-11	Syphilitic genital ulceration	Pregnant twenty times in twenty years; sixteen miscarriages, usually at two or three months	None
v-13	Chronic alcoholism, suspected tuberculosis	Chancre thirty-two years ago; rash twenty years ago; scars on penis, back and head	None
iii-1	Myocarditis; cardiac asthma	Chancre ten years ago; aneurism arch aorta	Arsphenamin 6 times, potassium iodid and mercury
iii-8	Syphilitic organic heart disease; general paresis	Perforated nasal septum; aortic regurgitation; tertiary syphilis; paresis, left side of face; cataract and posterior synechiae; aneurysmal dilatation of aorta	Syphilitic treatment, potassium iodid and mercury
iii-9	Cancer of stomach	Chancre four years ago; patellar reflex weak; gastric crisis	None
xii-58	Malaria	Chancre one year ago.....	None
xii-32	Hydrocele (syphilitic)	Chancre four years ago; secondary syphilis three years ago	None
xiii 23-50	Cerebrospinal syphilis	Chancre twenty-five years ago; loss of memory; scar on penis; drooping eyelids	None
xii-49	Chancre	Chancre three weeks ago.....	None
xiii-15	Acute epididymitis	Chancre three years ago; chronic gonorrheal urethritis; prostatic seminal vesiculitis and epididymitis	None
xiv-75	Cerebral syphilis	Chancre twenty-five years ago; Argyll Robertson pupils; spinal fluid examination: globulins + +, 80 cells	None
xiv-9	Traumatic epilepsy	Chancre twenty-four years ago; scar on penis and body	None

TABLE 3.—(Continued)

CASES IN WHICH THERE WAS NO COMPLETE RECORD AVAILABLE FROM HOSPITAL SOURCES, MOST OF THE SERUMS BEING OBTAINED FROM THE OUTPATIENT DEPARTMENT

	Clinical Diagnosis on Admission	Clinical History	Treatment
xii-49	History of chancre.....	None
xiii-15	Syphilis	History of chancre.....	None
i-55	Tertiary syphilis	None
ix-15	Fract. mandible	History of chancre.....	None
xii-4P	Syphilis	History of chancre.....	One injection
i-46	Tabes	None
v-11	Syphilitic ulcer of leg	None
xiv-2	Pulmonary tuberculosis and syphilis	History of chancre.....	None
i-6	Chancre on lip.....	None
i-9	History of chancre fifteen years ago.....	None
i-13	Syphilis	None
xiii-62P	Syphilis	Syphilis.....	Treated case

TWENTY CASES IN WHICH THE WASSERMANN REACTION WAS NEGATIVE BUT THE SACHS-GEORGI POSITIVE WITHOUT ANY EVIDENCE OF SYPHILIS ON THE PART OF THE PATIENT, EITHER IN THE HISTORY OR CLINICAL FINDING

	Diagnosis or Symptoms		Diagnosis or Symptoms
iv-10	Pain in legs; optic neuritis	xiii-4	Bronchitis; asthma
vii-69	Dementia praecox	xiii-1	Typhoid
vii-68	Chronic alcoholism	xiv-30	Chronic nephritis
viii-22	Routine; no diagnosis	xiv-33	Bilateral salpingitis
viii-15	Ovarian cyst	xiv-54	Chronic bronchitis
ix-28	Routine; no diagnosis	xiv-55	Suspected carcinoma of colon
xii-31	Routine; no diagnosis	xiv-29	Routine; no diagnosis
xiii-24	Lobar pneumonia	xiv-13	Cerebral hemorrhage
xiii-14	Acute cystitis	xiv-5	Constipation
xiii-10	Acute gonorrhea; lobar pneumonia	xvii	Chronic arthritis and myocarditis

In six serums obtained from the serologist of the City Health Department, we obtained a positive Sachs-Georgi reaction with a negative Wassermann. These serums are sent in without diagnosis and we have no information concerning them.

TABLE 4.—RESULTS OF SERUM TESTS

Reaction	Result								
	Positive			Negative			Doubtful		
Wassermann.....	+	±	—	+	±	—	+	±	—
Sachs-Georgi.....	5,808	282	514	686	221	15,950	154	246	325
Total.....	24,186								

the cases in which the Wassermann reaction was positive and the Sachs-Georgi negative or doubtful, numbered 1,121, or 51 per cent.; those in which the Wassermann was negative while the Sachs-Georgi was positive or doubtful numbered 1,061, or 48 per cent. These collected results represent the observations made with various modifications of technic, particularly in regard to incubation time. The cases in which

the Wassermann reaction was negative while the Sachs-Georgi was positive include a considerable number of treated cases of primary and parasyphilitic disease, of congenital syphilis, as well as a small group of diseases of nonsyphilitic basis. The latter may possibly be eliminated with further study of the preparation of the antigen. Just as the Wassermann reaction becomes nonspecific to a considerable degree when the antigen is fortified with too much cholesterol, so perhaps the acuity of the Sachs-Georgi reaction can be modified when once we become familiar with its range.

DISCUSSION

An examination of the results tabulated herewith makes it evident that this flocculation test very closely approximates the results obtained with the classical Wassermann reaction and may in some ways prove superior to it. While for the time being we must accept the Wassermann test as our standard of comparison, we should by no means lose sight of the fact that this standard is not infallible. While the error does not lie in the direction of nonspecificity, a definite number of positive syphilitic cases do not react with the Wassermann technic and are either classed as negative or yield doubtful readings. It seems that this relatively large group of cases flocculate quite readily with the Sachs-Georgi method, as will be apparent from a perusal of some of the histories and clinical findings recorded in Table 2. Only in thirty-two cases of the series were the Sachs-Georgi reactions positive in the absence of positive clinical findings or history.

We can enter here but briefly into a discussion of the mechanism that seems to underlie the flocculation made grossly apparent in the Sachs-Georgi reaction, and which is closely related to the ultramicroscopic colloidal alterations that have been described as taking place in the Wassermann reaction when the antigen is added to the serum. Both the globulins and the lipoids of the syphilitic serum seem altered to some degree, and Schmidt,⁷ Hirschfeld and Klinger,⁸ Sachs,⁹ and Meinicke¹⁰ are of the opinion that the alteration involves a peculiar lipotropic property of the serum globulins, the lipoglobulin aggregate being easily precipitated in solutions that are iso-electric for the globu-

7. Schmidt: *Ztschr. f. Hyg. u. Infektionskrankh.* **69**:513, 1911.

8. Hirschfeld and Klinger: *Ztschr. f. Immunitätsforsch.* **21**:40, 1914.

9. Sachs, H.: *Kolloid-Ztschr.* **24**:123, 1919.

10. Meinicke, E.: *München. med. Wehnschr.* **66**:932, 1919.

lins. Neukirch¹¹ places the hydrogen-ion concentration represented in a 0.85 per cent. salt solution as the optimum for the precipitation of the globulins, i. e., the identical concentration found most satisfactory for use in the Sachs-Georgi technic. From the point of view of its theoretical interest, we wish to call attention to the two phase reaction of Meinicke¹ for syphilis. This reaction involves the precipitation of the globulins of the serum in both negative and positive serums by simple dilution after the addition of antigen; then the addition of varying dilutions of salt solution to the serums so altered. In positive cases, the lipoglobulin precipitate remains unchanged; in negative cases the precipitates redissolve.

The Sachs-Georgi reaction is exceptionally simple, and once a suitable antigen has been prepared, it can be carried out with ease. The use of the complement-amboceptor-hemolytic system used in the Wassermann reaction is after all a cumbersome method of making apparent the colloidal alterations which are at the basis of these reactions for syphilis. Ultimately such a system must be replaced by a reaction simpler in character, requiring fewer reagents and less manipulation. Whether such a reaction will be of the flocculation type, such as the Sachs-Georgi, or will be purely chemical, is for the present not in the range of discussion. It is evident, however, that the Sachs-Georgi, reaction, even in its present form, offers a valuable contribution because of its simplicity and its apparent practicability. The fact, too, that it is frequently positive in those syphilitic cases which do not give a positive Wassermann reaction makes it of value as an additional test to be used in conjunction with the Wassermann technic. The fact that a relatively small percentage of nonspecific reactions is obtained should not detract from its ultimate usefulness; the earlier work with the Wassermann reaction was handicapped until the preparation of antigens was better understood.

CONCLUSIONS

An examination of 1,042 serums and cerebrospinal fluids by means of the Wassermann and the Sachs-Georgi reactions demonstrated a close parallelism of the two reactions (92 per cent.).

In sixty-two cases in which the Wassermann reaction was negative while the Sachs-Georgi reaction was positive or doubtful, the clinical history or examination revealed evidence of syphilis in 58 per cent.

The technic of the Sachs-Georgi reaction is simple, only one biologic reagent is required (antigen) instead of the four used in the Wassermann test (antigen, amboceptor, complement and red blood

11. Neukirch, P.: *Ztschr. f. Immunitätsforsch. u. exper. Therap.* **29**:498, 1920.

cells). This simplicity adds to the uniformity of the results. The ultimate specificity depends on the preparation of a proper antigen.

Because of its simplicity, and the fact that it is frequently positive in syphilitic cases when the Wassermann test is negative, we are of the opinion that the Sachs-Georgi reaction offers a valuable aid in the routine examination for syphilis when used in conjunction with the Wassermann reaction.

A SPURIOUS CHANCER

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The case reported has a double interest, because it illustrates how perfectly an initial sclerosis may be mimicked by a factitial or benign inflammatory lesion, and how critical one may justly be of accounts of reinfections, superinfections and cures based on the excision of the chancre when the diagnosis of the lesion has been made on clinical criteria alone, without a complete confirmation by dark-field and serologic examination.

REPORT OF A CASE

History.—The case of C. P. (Case 295316) was diagnosed as tabes dorsalis, following an examination at the clinic in November, 1919. The spiral fluid Wassermann reaction was positive, the Nonne reaction was positive, and the lymphocytes numbered 140. The patient received six intravenous injections of arsphenamin, twenty intramuscular injections of mercury succinimid and interim treatment of forty mercurial inunctions. The patient, although repeatedly questioned, could give no history of a primary lesion, his first intimation that he had syphilis being in 1909, when his hair fell out in large amounts, and a quack told him that he had the disease. There was no sign of penile scar on first examination.

In June, 1920, this patient returned for further treatment. Supposing himself to be immune from the disease by virtue of having had syphilis, he had had a single intercourse with a clandestine prostitute six weeks before. Fourteen days later a papule appeared on the prepuce behind the corona, enlarging to half the size shown in the photograph and developing a superficial erosion before he gave it any attention. He then visited a physician who cauterized it twice with some mild chemical cauterant. The patient insisted that the only difference between the appearance of the lesion when cauterized and its appearance at the time of examination was in size.

Examination.—Examination disclosed the apparently typical initial sclerosis shown in the illustration. The base was smooth, the border faintly hemorrhagic, the exudate perhaps a trifle purulent, but serous after wiping with gauze. The induration was of the button type. There was no distinct inguinal adenopathy, although the discrete glands were palpable.

Three dark-field examinations were negative, two of them after saline soakings and one of them on aspiration of the base of the lesion. The Wassermann reaction of the blood was negative. The lesion was then excised and half of it sent to Professor A. S. Warthin of Ann Arbor, who reported that the pathology was that of a simple inflammatory reaction, not at all suggestive of syphilis, and that no *Spirochaeta pallida* could be identified in the tissue. In the meanwhile, an examination of the spinal fluid yielded positive Wassermann and Nonne reactions, 134 lymphocytes, and a colloidal gold curve of 0112222100.

The prostitute by whom the patient had been exposed was not accessible. Had she had active syphilis, with spirochete-containing lesions in the vagina, it is conceivable that the lesion in the patient might have been an inoculation gumma, since gumma-like lesions can be produced by the inoculation of living *Spirochæta pallida* into the skins of patients with late syphilis.¹ The lesion could scarcely be interpreted clinically as a pseudochancere-redux in view of the previous



A spurious chancre with typical incubation, probably due to trauma and cauterization, in a patient with neurosyphilis.

treatment and in the absence of evidence of a former primary lesion at the same site or in its lymphatic drainage. The pathologic examination seems to eliminate both possibilities, as well as that of a superinfection. The lesion was evidently purely inflammatory, possibly in part at least an artefact due to cauterization. The perfection with which this spurious chancre mimicked the true Hunterian induration emphasizes the untrustworthiness of clinical, as distinguished from laboratory, criteria in the diagnosis of primary syphilis and in the determination of the status of reinfections and superinfections.

1. Landsteiner and Finger: Ueber Immunität bei Syphilis, Centralbl f. Bakteriöl. **38**: Suppl. 107, 1906.

Correspondence

ARTIFICIAL LIGHT FOR PHOTOGRAPHY

To the Editor:—The difficulties of getting sufficient light for the taking of clinical photographs of dermatologic interest, which is feasible for office use, led me to try the air cooled mercury quartz lamp, which has become a fixture in almost all dermatologists' offices. My success has far exceeded expectations. I have not found any source of light which approaches it in intensity, and, except for the wearing of the protective goggles, gives as much ease of manipulation and is as free from objectionable features. Speed of exposure, which is a necessary factor for good photographs, is assured with the lamp. The lens may be stopped down, which aids in giving depth to the picture. There is no attendant explosion, and no smoke to upset the office or to make further stay in the room impossible for more pictures or other purposes. (If a smoke bag is used, light is cut down.)

As far as I know, the mercury quartz lamp has not previously been delegated for such lowly function. Perhaps others may find that it solves their lighting problem for clinical photographs.

HERMAN GOODMAN, M.D., New York.

Abstracts from Current Literature

TUBING AS A CAUSE OF REACTION TO INTRAVENOUS INJECTION, ESPECIALLY OF ARSPHENAMIN. JOHN H. STOKES and G. J. BUSMAN, J. A. M. A. **74:15** (April 10) 1920.

The writers investigated the cause of an arsphenamin reaction, characterized by a chill with a sharp rise in temperature coming on from thirty minutes to one hour after intravenous injection, accompanied by nausea, vomiting, diarrhea, pain in the head and back and varying degrees of prostration. This reaction appeared in crops, so to speak, and then disappeared for a considerable period, only to recur in the midst of what appeared to be a period of flawless technical accuracy.

It was finally determined that this reaction resulted from the employment of a certain widely distributed brand of so-called pure gum rubber tubing. The tubing, when new, appears to contain a toxic agent responsible for the reaction. The toxic substance gradually disappears from the tubing on use, and may be removed in the first instance by soaking the tubing for six hours in normal sodium hydroxid solution and rinsing. The toxic property is not destroyed in the ordinary process of sterilization by boiling (from one-half to one hour), is not soluble in water or removable by irrigation, appears in toxic amounts in arsphenamin, neo-arsphenamin and dilute sodium hydroxid solution merely on passing them through a new tube en route from container to vein, and apparently is not associated with the mechanically removable debris from the inner surface of the tube.

LEVIN, New York.

THE FREQUENCY WITH WHICH VARIOUS LOCALITIES ARE ATTACKED BY LUPUS VULGARIS. CARL WITTH, Brit. J. Dermat. & Syph. **32:287**, 1920.

Compiling statistics from 897 cases of lupus vulgaris, in which 665 patients were above 16 years of age, 116 between the ages of 11 and 16, and 116 below 11 years of age. Witth gives the frequency of lupus in various sites at various age periods. His findings confirm the old observations regarding the frequency of lupus on and in the nose, the way in which one attack depends on the other, and regarding the lymphoma on the neck playing the greatest rôle for the lupus in that site. It has been demonstrated that lupus on and in the nose, compared with lupus on the center of the cheek, is comparatively rare in children, but increases between the ages of 11 and 16; and the comparative frequency of lupus on the extremities during childhood is confirmed.

SENEAR, Chicago.

EYE LESIONS PRODUCED BY LIGHT RICH IN ULTRAVIOLET RAYS. J. VAN DER HOEVE, Am. J. Ophth. **3:178** (March) 1920.

The writer states that nearly every part of the eye is susceptible to damage by undue exposure to natural or artificial light rich in ultraviolet rays. The cornea and lens in particular show a selective absorption for these rays and whether the superficial or deep parts of the eye are affected depends on

the wave length of the rays, those of shorter wave length being more readily absorbed. The most frequent affection is photophthalmia, characterized by intense photophobia and lacrimation with sometimes blepharospasm and ciliary neuralgia. Other conditions are acute conjunctivitis, iritis and keratitis, senile cataract and senile degeneration of the macula. Snow blindness is cited as an affection of this character due to natural light rich in ultraviolet rays, while as artificial causative agents are mentioned the mercury vapor lamp, arc lamp, electric welding and short circuit flashes. The writer does not consider short therapeutic exposures with the Kromayer mercury vapor lamp as distinctly harmful, especially when the pupillary part is not directly exposed.

CULTURAL STUDIES ON A CASE OF SPRUE. WADE W. OLIVER, J. A. M. A. **74**:27 (Jan. 3) 1920.

Oliver reports laboratory studies on a case of sprue—that of an American invalided to Brooklyn from Porto Rico:

From the stool, from tongue scrapings, from sputum and from tooth abscess, a growth of yeasts was obtained which corresponded in the main to *Monilia psilosis*, described by Ashford as the cause of sprue.

Morphology.—The yeast exhibited a striking variation in size and form, which seemed somewhat independent of the medium, as a mount made from a single colony showed a polymorphism among its members. The single cells were round or oval, varying in diameter from about 2 to 7 microns, were sharply defined in outline, and possessed a nucleus which was recognizable in fresh preparations. Many cells showed an oval or spherical, faintly outlined vacuole. Mycelial elements were constantly observed in +1 glucose agar but best apparently in gelatin.

A guinea-pig was inoculated with an agar culture of this organism. Death occurred in seven days. Postmortem examination revealed a large abdominal abscess involving various organs.

From the gall bladder, as well as from a liver abscess, *Monilia* was recovered, in culture mixed with *Staphylococcus aureus*.

CLARK, Chicago.

DERMATITIS DUE TO CARPOGLYPHUS PASSULARUM. W. J. O'DONOVAN, Brit. J. Dermat. & Syph. **32**:297, 1920.

O'Donovan reports the case of a man, who, while shoveling dried figs, developed over the forearms, backs of the hands and on the face an eruption of discrete, closely set, apparently follicular papules, pale pink in color with red scabbed tops. The lesions were suggestive of scabis, but were too small, and there was no evidence of burrowing.

Examination of the figs showed them to be covered with a fine, light brown powder, which microscopic examination disclosed was made up of live and dead mites and numerous fragmented particles of acari and their limbs. The parasite was identified as *Carpoglyphus passularum*. The author states that Rasch had previously described two cases of dermatitis due to the Carpo-glyphus occurring among workers who had been handling dried plums.

SENEAR, Chicago.

CASE OF ACUTE LUPUS ERYTHEMATOSUS. E. G. GRAHAM LITTLE, Proc. Roy. Soc. **2**:3 (Sept.) 1920.

A case report.

GUY, Pittsburgh.

RADIUM IN THE TREATMENT OF DISEASES OF THE EYE AND ADNEXA. G. B. NEW and W. L. BENEDICT, *Am. J. Ophth.* **3**:245 (April) 1920

The writer's observations were drawn from a series of 133 cases, of which ninety-seven were basal cell epitheliomas of the lids and canthus. Radium was used in the unscreened plaque and silver tube without additional screening other than rubber tissue. The dosage was uniformly heavy for the malignant lesions and in many cases it was carried out over a period of several days. Five case reports were submitted in which the dosage and mode of application were definitely stated. Blastomycosis, vernal catarrh and the angiomas were among the lesions considered favorable for radiotherapy. The thorough use of the knife or cautery preceding the application of radium was advised for melanotic sarcoma, glioma, squamous cell epithelioma, and those cases of basal cell epitheliomas infiltrating deep tissues or involving bone.

UEBER ZWEI FALLE VON NEURODERMITIS NODULOSA (GROSZ-NOTIGE FORM DER NEURODERMITIS BROCC) (TWO CASES OF NEURODERMITIS NODULOSA). J. FABRY, *Arch. f. Dermat. u. Syph.* **121**:241 (April) 1915.

Two cases are reported. The first one was described by the author in 1895 as urticaria papulosa perstans. Now, after many years of study, he believes the case is one of neurodermitis of Brocq.

The lesions were pigmented papules about 0.5 cm. in diameter, with a thin scale. New lesions were red while the old ones were dark gray in color. There was leather-like thickening with lichenification. The entire skin was of a grayish color. There was no tendency to urticarial lesions. The patients suffered with intense persistent itching. Treatment was of no avail.

HEITHAUS, Cleveland.

CLINICAL NOTE. CHRYSAROBIN AS A CAUSE FOR PSORIASIS.

E. WARD, *Brit. J. Dermat. & Syph.* **32**:299, 1920.

Ward cites a case in which a man who had used chrysarobin ointment successfully for many years in the treatment of psoriasis, doubled the strength of the ointment. The lesion cleared up in the usual way, but fresh papules appeared in a circle at the inner margin of the red zone produced by the treatment. A milder chrysarobin ointment removed the new papules successfully.

SENEAR, Chicago.

REPORT OF A CASE OF GENERALIZED PSORIASIS AND AMENORRHEA CURED WITH OVARIAN EXTRACT. G. VERROTTI, *Riforma med.* **36**:321, 1920.

Verrotti reports the case of a woman, 29 years old, who for six years had been suffering from a stubborn psoriatic eruption. Her menses had been scanty since the beginning of the dermatosis and had finally disappeared entirely. In spite of all kinds of local treatment, the disease remained practically unchanged until the author decided to give the patient ovarian extract. The eruption vanished in a short time, menstruation returned and the patient has remained well for eighteen months.

PARDO-CASTELLO, Havana.

DES FORMES ABORTIVES DE LA MALADIE DE RECKLINGHAUSEN
(THE ABORTIVE TYPES OF RECKLINGHAUSEN'S DISEASE).C. ADRIAN and G. HÜGEL, *Ann. de dermat. et syph.* **7**:152 (May) 1919.

Adrian and Hügel report two cases of the disease with irregular disseminated patches of pigmentation, without tumors and nerve involvement. One of the patients subsequently developed about a dozen tumors the size of peas, situated on the chest and thighs.

BECHET, New York.

LES LOCALIZATIONS HORS DES PLIS DE L'EPIDERMOPHYTON
INGUINALE (THE LOCALIZATION OF THE EPIDERMOPHYTON
INGUINALE, OTHER THAN IN THE FOLDS). PAUTRIER, *Ann. de
dermat. et syph.* **7**:278 (Sept.) 1919.

The author reports two cases of eczema marginatum, with lesions scattered over the legs and trunk, in which *Epidermophyton inguinale* was demonstrable.

BECHET, New York.

SPECIALE COMPORTAMENTO DEL LIQUIDO CEFALO-RACHIDIANO
NELLA NEUROSIFILIDE PER LA PRESENZA DI ANTICORPI
SPECIFICI TERMOLABILE (BEHAVIOR OF THE SPINAL FLUID
IN SYPHILIS OF THE NERVOUS SYSTEM DUE TO THE PRES-
ENCE OF THERMOLABILE SPECIFIC ANTIBODIES). C. Rizzo,
Lo Sperimentale **74**:1 (January-June) 1920.

The author reports that in his experience the spinal fluid inactivated at a temperature of 56 C. may give a negative Wassermann reaction, while if used active, it gives a positive test. He says that the spinal fluid should never be inactivated, as it contains thermolabile specific antibodies which are destroyed by heat.

PARDO-CASTELLO, Havana.

STIGMATA OF PREDISPOSITION TO BONE AND JOINT TUBERCLE.

W. C. RIVERS, *Brit. J. Child. Dis.* **199-201**:140 (July-Sept.) 1920.

English schoolchildren were the objects of this investigation. As a result of observations in 353 tuberculous cases as compared with 610 normal controls, it was concluded that in bone and joint tuberculosis red and reddish hair is nearly twice as frequent as in the ordinary population (7 per cent. as compared with 3.4 per cent.). Probably also a tendency to permanent freckling is a little commoner in those with bone and joint tuberculosis than in normal children. Again, in 421 cases, contrasted with 324 "controls," it was found that ichthyosis is seen at least twice as frequently in afflicted as in nontuberculous children. In view of the possible atavistic nature of red hair and ichthyosis, these findings are of interest.

PARKHURST, New York.

HEREDITARY SYPHILITIC AORTITIS. E. J. STOLKIND, *Brit. J. Child.
Dis.* **199-201**:126 (July-Sept.) 1920.

In a search of the literature the author has been unable to find any cases in which *Spirochaeta pallida* has been found in the aorta of children with

hereditary syphilis, aged more than 1 year. Authors so far are not agreed as to the typical pathologic changes of hereditary syphilis in the aorta of fetuses and new-born infants, and this question needs further investigation. On the other hand, the lesions of syphilitic aortitis in adolescents and adults are characteristic. There is given a brief outline of the cases of alleged hereditary syphilitic aortitis, with the author's conclusion that he has so far been unable to find in the literature a single case of proved hereditary syphilitic aortitis, though such cases may exist. Further researches are needed.

PARKHURST, New York.

UN CAS DE DERMATITE DE DUHRING PUSTULEUSE (A CASE OF DUHRING'S DISEASE WITH PUSTULAR LESIONS). MILIAN, *Ann. de dermat. et syph.* **7**:193 (July) 1919.

The author comments on the rarity of primary pustular lesions in dermatitis herpetiformis, and reports an example of this particular type of eruption.

BECHET, New York.

UEBER MANIFESTATIONEM DER LUES AM AUGEN BEI POSITIVEM LIQUORBESUND (MANIFESTATIONS IN THE EYE OF SYPHILITIC PATIENTS WITH POSITIVE FINDINGS IN THE CEREBROSPINAL FLUID). L. STROSS and A. FUCHS, *Wien. klin. Wchnschr.* **33**:986, 1920.

The authors undertook to study the eye in all cases from Kyrle's clinic in which there were positive findings in the spinal fluid. They tabulate the findings:

POSITIVE CEREBROSPINAL FLUID FINDINGS

	Men	Women	Total
Early syphilis, positive eye findings....	6	11	17
Early syphilis, negative eye findings....	14	18	32
Late syphilis, positive eye findings.....	12	7	19
Late syphilis, negative eye findings.....	9	7	16

The relative involvement of the eye in the early and late cases, and in men and women may be learned from this table.

No attempt is made to formulate percentage tables, etc., because only by long continued studies over long periods of time will the relationship between positive findings in the spinal fluid of syphilitic patients and disease of the eye be fully understood.

GOODMAN, New York.

REVIEW OF UNTOWARD EFFECTS FOLLOWING ARSPHENAMIN AND ITS DERIVATIVES. W. P. BOARDMAN, *Boston M. & S. J.* **183**: 561 (Nov. 11) 1920.

The author reviews recent literature on the subject, citing two fatal cases, one from exfoliative dermatitis and the other from acute yellow atrophy of the liver. Various complications are discussed in more or less detail, as well as certain of the contraindications.

LANE, Boston.

CHRONIC FIBROID SUBCUTANEOUS SYPHILOMATA OF THE LEGS, ASSOCIATED WITH CHRONIC PERI-URETHRAL INDURATION IN THE PENIS. F. PARKES WEBER, *Proc. Roy. Soc. Med.* **13**:9 (July) 1920.

Multiple subcutaneous painless hard nodules on the legs below the knees, with one similar lesion on the outer side of the right thigh and another in the distal half of the penis, in a patient with a positive Wassermann reaction, were found to be composed of masses of fibrous tissue with numerous foci of chronic inflammation. The condition was little affected by specific therapy or fibrolysin. In a discussion Dr. McDonagh spoke of the condition as "induratio penis plastica," which he stated was never due to syphilis, but in over 50 per cent. of cases it was associated with glycosuria or hyperglycemia. He ascribed the condition to "acidness" of the blood and stated that in early cases colloidal iodine and intramin would bring about its dissolution.

Guy, Pittsburgh.

RADIUM IN DERMATOLOGIC PRACTICE. LOUIS B. MOUNT, *Urol. & Cutan. Rev.* **24**:10 (Oct.) 1920.

The greatest use of radium is in epithelioma of the skin. Healing is obtained with slight inconvenience to the patient, no discomfort of any moment, and with cosmetic results unobtainable by any other means. Other cutaneous conditions in which it is recommended are: keloids and keloidal scars, acne keloid, keratoses and preepitheliomatous lesions, plantar warts, verrucae and papillomas, chronic eczema, lymphangioma circumscriptum, lupus vulgaris, lupus erythematosus and cheilitis exfoliativa.

LEVIN, New York.

THE PREPARATION OF AMBOCEPTOR WITH HUMAN ERYTHROCYTES. A. H. SANFORD, *Am. J. Syph.* **4**:697 (Oct.) 1920.

The author employed the human erythrocytic hemolytic system and found that its chief disadvantage, that is, removal of the natural hemagglutinins from the amboceptor, may be eliminated by using dogs for developing the amboceptor. Small dogs are most suitable. From 30 to 60 c.c. of a 50 per cent. suspension are injected intraperitoneally at intervals of one week. From 3 to 5 injections are required.

The amboceptor obtained has a comparatively low titer, averaging about 1:500.

TOMLINSON, Omaha.

CASE OF 1. LUPUS ERYTHEMATOSUS (ANOMALOUS TYPE).
2. FOLLICULITIS ULERYTHEMATOSA RETICULATA OF McKEE.
H. C. SAMUEL, *Proc. Roy. Soc.* **2**:3 (Sept.) 1920.

1. Lupus erythematosus or folliculitis ulerythematosus of McKee. This case exhibited telangiectases followed by superficial scarring in the form of reticulate pitting and affecting the flush areas of the face. A family history of tuberculosis was noted, and the patient had an evident weak circulation. The age of the patient (34) and absence of comedones were considered against the second diagnosis.

Guy, Pittsburgh.

FUNKTIONSSTOERUNGEN DES SYMPATIKUS. KRIESSAERTZLICH-
DERMATOLOGISCHE BEOBACHTUNGEN (DISTURBANCE OF
THE FUNCTION OF THE SYMPATHETIC. WAR OBSERVA-
TIONS IN DERMATOLOGY). OSCAR SPRINZ, Arch. f. Dermat. u.
Syph. **123**:894, 1916.

In this article the author gives a review, and recounts his personal experience with dermatologic diseases following injury from war wounds to the sympathetic nervous system. Addison's disease, herpes zoster gangrenosus, hypertrichosis, and disturbances of the pilomotor and secretory functions of the skin have followed injuries to the sympathetic nervous system. Changes in nail growth are also mentioned.

GOODMAN, New York.

LUES UND KARZINOM (SYPHILIS AND CARCINOMA). GUSTAV
STÜMPKE, Arch. f. Dermat. u. Syph. **123**:1082, 1916.

Stümpke adds a case of a relationship between syphilis and carcinoma to those already well known. He mentions the existence of carcinoma on the basis of late skin manifestations of syphilis, on scars, on the site of chancre and on leukoplakial degeneration.

The case history given is not convincing.

GOODMAN, New York.

A STANDARDIZED METHOD OF PERFORMING THE WASSER-
MANN REACTION. WILLIAM A. HINTON, Am. J. Syph. **4**:598 (Oct.) 1920.

The author reports a standardized method for performing the Wassermann reaction which has been quite generally adopted in Massachusetts. He gives a detailed description of his technic, including the preparation of all materials used.

TOMLINSON, Omaha.

CHOLESTERINEMIA AND THE WASSERMANN REACTION. EDWIN
HENES, JR., Am. J. Syph. **4**:685 (Oct.) 1920.

On account of the varying degrees of cholesterinemia found in different patients, the author does not consider a cholesterinized antigen reliable unless the cholesterin content of the blood has been determined. He considers it important to determine the cholesterin content of the blood if we are to obtain reliable Wassermann reactions.

TOMLINSON, Omaha.

UEBER ZWEI FAELLE VON CONJUNCTIVO-KERATITIS GONOR-
RHOICA (TWO CASES OF CONJUNCTIVO-KERATITIS GONOR-
RHOICA). J. W. VAN DER VALK, Acta Dermat.-Vener. **1**:254 (Oct.) 1920.

The differences between the parakeratotic papule of gonorrhea and the erosive lesions under the prepuce and on the eye are probably due solely to their great differences in moisture and protection.

Reviewing the literature concerning the mode of origin of these lesions, the author concludes that, instead of being blood borne, it is quite possible that the causative agent, be it organism or toxin, may follow the nerve fibrils. The corneal distribution of the condition in his two cases suggested this.

PARKHURST, New York.

CASE OF CHRONIC DIPHThERITIC GRANULOMA. F. G. GRAHAM
LITTLE, Proc. Roy. Soc. **2**:3 (Sept.) 1920.

An officer serving in France developed medallion-like lesions, with warty centers and ulcerating edges, on the right side of the right foot, the dorsum of the toes of the left foot, on the left shoulder and at the orifice of the left nostril. The hard palate and the fauces were similarly affected. An organism closely resembling the Klebs-Loeffler bacillus was found, but on account of the fact that the patient had had several attacks of gonorrhea the possibility of a gonorrheal hyperkeratosis was considered, this being considered unlikely on account of the mucous membrane involvement.

Guy, Pittsburgh.

UEBER DAS VERHALTEN DER WASSERMANNSCHEN REAKTION
BEI TUBERKULIDEN (CONCERNING THE POSITION OF THE
WASSERMANN REACTION IN TUBERCULIDS). OTTO SACHS,
Arch. f. Dermat. u. Syph. **123**:838, 1916.

The Wassermann reaction has been reported positive in a number of cases of tuberculid, and Sachs has had two cases. Other cases of tuberculid have given the negative reaction. One must make a careful inquiry into the antecedent history for the possibility of syphilitic infection, as well as make a complete physical examination. Only after a long study of many clinical cases will any worthy conclusions be reached. The effort will not only add to the significance of the tuberculids, but it is necessary to maintain the position of the Wassermann reaction.

GOODMAN, New York.

THE DIAGNOSIS OF PRIMARY SYPHILIS. H. D. LLOYD, Boston M. &
S. J. **183**:540 (Nov. 4) 1920.

A discussion of the clinical, dark-field and serologic diagnosis of early syphilis is presented. The author emphasizes the early use of the dark-field examination, quoting a series in which a positive diagnosis was made in 96 per cent. of the cases by means of the dark field.

LANE, Boston.

A CASE OF DELHI BOIL OR SORE. J. H. STOWERS, Brit. J. Dermat.
& Syph. **32**:263 (Aug.-Sept.) 1920.

As a clinical note, Stowers reports a case of Delhi boil seen in England. The patient, a woman aged 34 years, had resided in India for the past nine years. There were two nodules below the right eye, and a third on the left forearm. The parasite, *Leishmania tropica*, was easily demonstrated by Dr. Castellani.

SENEAR, Chicago.

DIE THERAPEUTISCHE ANWENDUNG DER KUENSTLICHEN
HOEHENSONNE IN DER DERMATOLOGIE (THE THERAPEU-
TIC APPLICATION OF THE ARTIFICIAL SUN LAMP IN DERMA-
TOLOGY). G. SCHERBER, Arch. f. Dermat. u. Syph. **123**:843, 1916.

Pemphigus vulgaris, dermatitis herpetiformis, chronic granulating wounds, ulcers of tuberculosis, ulcers of the leg, lichen rubra acuminatus, prurigo and

scleroderma have been distinctly benefited by the use of the artificial sun rays. The treatment is of greatest benefit if used in conjunction with other means of therapy, for example, arsenic, tuberculin injections and other therapeutic measures, as indicated.

GOODMAN, New York.

THE PREVENTION OF VENEREAL DISEASE BY IMMEDIATE SELF-DISINFECTION. H. WANSEY BAYLY, *Internat. J. Surg.* **33**:213 (July) 1920.

The author believes that failure of disinfection methods is due to lack of proper material and knowledge of its use rather than to the antiseptics themselves. This method also is of much less value to women than to men. The author favors venereal prophylaxis for both men and women at the earliest possible moment after exposure, using 33 per cent. calomel ointment and 1:1,000 potassium permanganate.

JAMIESON, Detroit.

CONSERVATION DU REFLEXE OCULO-CARDIAQUE DANS L'HEREDO SYPHILIS MEME COMPLIQUEE D'AORTITE. AVEC UNE OBSERVATION D'INSUFFISANCE AORTIQUE TRAUMATIQUE CHEZ UN HEREDO-SYPHILITIQUE (CONSERVATION OF THE OCULOCARDIAC REFLEX IN TRUE HEREDO-SYPHILIS COMPLICATED WITH AN AORTITIS. REPORT OF A CASE OF TRAUMATIC AORTIC INSUFFICIENCY IN A HEREDOSYPHILITIC). MOUGEOT, *Ann. de dermat. et syph.* **7**:157 (May) 1919.

Mougeot concludes from a study of the subject that the oculocardiac reflex in a large majority of cases of hereditary syphilis remains intact. It is absent in one half of the cases of acquired secondary syphilis, and in four fifths of the cases of tertiary syphilis without demonstrable nervous involvement. It is almost entirely absent in cerebrospinal syphilis.

BECHE, New York.

DIE PUNKTION DES RUECKENMARKKANALE (LUMBALPUNKTION) IN DER DIAGNOSE UND THERAPIE DER SYPHILIS (LUMBAR PUNCTURE IN THE DIAGNOSIS AND TREATMENT OF SYPHILIS). CARL STERN, *Arch. f. Dermat. u. Syph.* **123**:943, 1916.

This monograph of about 120 pages deals with the history of lumbar puncture, the anatomy of the parts involved, the technic of the operation and studies of the normal and abnormal fluids. There is a critical analysis of the literature on cell counting, the origin of the cells in the fluid, the Nonne-Apelt Phase 1 reaction, globulin, the colloidal gold reaction of Lange, the Wassermann reaction and its significance, pathologic anatomy of early syphilitic meningitis, clinical relation to fluid findings, death following puncture, technic and results of intraspinal arsphenamin and the demonstration of spirochetes in the fluid. A statistical summary of the reported lumbar punctures and conclusions reached by a study of about 1,200 studies on the fluid (200 personal cases) closes the paper. The conclusions are those of 1916, and are of historical interest. The bibliography occupies five closely printed pages.

GOODMAN, New York.

YPERITES GENITALES SIMULANT LA SYPHILIS, ET SYPHILIS MASQUEE PAR YPERITE (YPERITE GAS BURNS OF THE GENITALIA SIMULATING SYPHILIS AND MASKED SYPHILIS FROM YPERITE BURNS). GOUGEROT and CLARA, *Ann. d. mal. vénér.* **14**:258 (May) 1919.

The authors state that gas burns of the genital region alone, or as a part of a general burn, had frequently been observed by them. The lesions frequently simulated primary syphilis, and occasionally masked the beginning of syphilis. The burns often cause an extensive phimosis or paraphimosis, with subpreputial inflammation and induration of the inguinal glands. Evolution alone eliminates the possibility of an associated syphilis. The authors report a number of cases.

BECHET, New York.

THE TREATMENT OF BILHARZIASIS WITH ANTIMONY. J. E. R. McDONOUGH, *J. Trop. M.* **23**:165 (July 1) 1920.

The author has found tartar emetic to be the best drug for intravenous use, having it prepared in ampules containing 1 c.c. of distilled water and 1½ grains of the drug. The contents are diluted up to 100 c.c. before injection. Injections are repeated every five days for ten doses.

JAMIESON, Detroit.

THE DEVELOPMENT OF COSMETIC RHINOPLASTY. SEYMOUR OPPENHEIMER, *New York State J. M.* **20**:355, 1920.

The author refers to various surgeons who, from the earliest times, have undertaken this operation, and pleads for the recognition of rhinoplasty as a legitimate and often necessary procedure. There is no discussion of technic or results.

WILLIAMS, New York.

PROGNOSTIC DES CHANCRES EXTRA-GENITAUX (THE PROGNO-SIS OF EXTRA-GENITAL CHANCRES). DUJARDIN, *Ann. de dermat. et syph.* **7**:221 (July) 1919.

The author concludes from a study of fifty-three extragenital chancres that the prognosis in no way differs from the genital chancre, thereby corroborating Fournier's dictum.

BECHET, New York.

LES ARHYTHMIES DE LA SYPHILIS SECONDAIRE (THE ARRHYTHMIAS IN SECONDARY SYPHILIS). DuCASTEL, *Ann. d. mal. vénér.* **14**:263 (May) 1919.

DuCastel states that he has frequently observed, both by touch and sphygmograph, irregularity of the pulse in secondary syphilis. Tachycardia was not frequent; only fifteen of fifty syphilitic patients had a pulse beat higher than 90. Arterial tension was below normal. In patients suffering from tachycardia, the pulse was soft, compressible and dicrotic. There was some precordial distress. He concludes that the arrhythmias in secondary syphilis have no grave significance, and almost invariably disappear in time.

BECHET, New York.

SURGICAL ASPECTS OF THE CHARCOT JOINT AND OTHER SYPHILITIC BONE AND JOINT LESIONS. FREDERIC J. COTTON, *Ann. Surg.* **72**:488 (Oct.) 1920.

The poor results usually experienced in the surgical treatment of charcot joints is probably due to their being handled as a purely surgical condition without due regard to the syphilitic element.

The author, in reporting results in his cases, recommends active anti-syphilitic treatment prior to surgical measures.

TOMLINSON, Omaha.

DIE KUTIREAKTION BEI LEPROA UND IHRE BEZIEHUNG ZUM LEPROAERYSIPELOID (DERMAL REACTION IN LEPROSY AND ITS APPLICATION TO ERYSIPELOID ATTACKS IN LEPROSY). ROBERT OTTO STEIN, *Arch. f. Dermat. u. Syph.* **123**:908, 1916.

Stein utilized lymph nodes from a lethal case of leprosy to make an antigen which he used for an intradermal test for the disease. Positive reactions were secured in cases of leprosy that showed erysipeloid attacks. Stein thinks that malignant syphilis among syphilitics, papulonecrotic tuberculids among the tuberculous, and erysipeloid attacks among the lepers are analogous results of a hypersensitiveness to the causative virus.

GOODMAN, New York.

LICHEN PLANUS. S. E. DORE, *Proc. Roy. Soc.* **2**:3 (Sept.) 1920.

A woman, aged 43, had two patches on the shins composed of closely set, acuminate, hard papules on a thickened skin, which was sepia colored. At the margins, the papules, which were not follicular, were arranged in rows.

GUY, Pittsburgh.

LA QUESTION DES APPAREILS DE VERRE DANS LES ACCIDENTS DU NEO-SALVARSAN (THE ROLE PLAYED BY GLASSWARE IN THE ETIOLOGY OF NEO-ARSPHENAMIN ACCIDENTS). J. GOLAY, *Ann. de dermat. et syph.* **7**:299 (Sept.) 1919.

The author is convinced that a small amount of neo-arsphenamin solution remains adherent to the glassware in spite of repeated washing, sterilization and disinfection. A part of this old oxidized neo-arsphenamin is taken up in solution at the next injection, thereby causing grave accidents. Golay, therefore, recommends repeated washings, and the testing of the washings with a 2 per cent. or 4 per cent. solution of silver nitrate. In the presence of even the minutest particles of arsenic there is a blackish or violaceous brown precipitate. The reaction is one of great delicacy, occurring in a solution of neo-arsphenamin as weak as one part in 100,000,000.

BECHET, New York.

SURGICAL TREATMENT OF ULCUS TROPICUM. ROBERT HOWARD, *J. Trop. M.* **23**:215 (Sept. 1) 1920.

Thorough curetting and removal of the undermined edge are recommended as the method of choice in treating this condition.

JAMIESON, Detroit.

DERMATOLOGIC ABSTRACTS

THE JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION

GASTRIC ANALYSIS IN ACNE ROSACEA. J. A. RYLE and H. W. BARBER, *Lancet* 2:1195, 1920.

A number of cases of acne rosacea were examined by Ryle and Barger with a view to determining, if possible, the actual pathogenesis of the condition and the most satisfactory method of treatment. The connection between this disease and dyspnea is generally recognized, and it is usually supposed that overindulgence in alcohol, tea, or coffee produces its effect by setting up a chronic gastritis. Twelve cases of acne rosacea were investigated by the fractional method of gastric analysis. In five there was complete achlorhydria throughout the period of the meal. In two cases there was an extreme degree of hypochlorhydria. Of the remaining five cases, one showed no secretion of free hydrochloric until after one hour, and two showed a temporary high peak in the curve of acidity, with an abrupt fall to the base line. Other features revealed by the test were a tendency to rapid emptying, such as obtains in other cases of so-called achylia gastrica, and a highly mucoid resting secretion, frequently of the viscid consistency of raw eggwhite. The increased liability to acne rosacea during menstrual period and pregnancy is of interest, in view of the fact that achylia is also reputed to be more common at these times. The administration of dilute hydrochloric acid, 30 minutes and upward, well diluted, after meals or during meals, has yielded very satisfactory results.

Society Transactions

NEW YORK DERMATOLOGICAL SOCIETY

Regular Meeting, Nov. 23, 1929

JAMES MCF. WINFIELD, M.D., *President*

ACNITIS. Presented by DR. WINFIELD.

A young man, aged 20, was always healthy until May, 1920, when he had an attack of appendicitis. He was ill for nearly a month. The appendix was not removed; the treatment consisted of application of ice bags. On recovery he noticed a number of small papules scattered over the nose, forehead and chin; some of them enlarged and broken down, which on healing left scars. The patient stated he had never had any previous skin eruption, such as acne or comedones. When Dr. Winfield first saw the patient there were a great many acne-like lesions scattered over the face and scalp. Some of them on the face resembled molluscum contagiosum; many of the papules had ulcerations; all had left scars. Those over the scalp and bearded portions of the face were accompanied by loss of hair. In addition to the papules, there were a number of deep seated nodules, especially about the neck. The case was shown because the acnitis had followed an attack of appendicitis in a subject who had always been in perfect health. The Wassermann test was negative, as was the tuberculin test.

The young man was of slender build and rather narrow chested. He had not been passed by the army examining board on account of questionable signs in the chest, although at present nothing was found on physical examination. Dr. Winfield was inclined to think the tuberculous focus was in the appendix.

DISCUSSION

DR. TRIMBLE agreed with the diagnosis. He had seen the patient previously in consultation. At that time he presented the exact picture shown at present, though there were many small lesions and hardly any large ones.

The case seemed to belong to the category of Barthélemy's acnitis, one of the synonyms of necrotic granuloma. He had been much interested in the history which showed that the condition followed an attack of appendicitis.

CASE FOR DIAGNOSIS. (MYCOSIS FUNGOIDES, LEUKEMIA CUTIS, IDIOPATHIC ATROPHY, ACRODERMATITIS ATROPHICANS?)

Presented by DR. LANE.

The patient, A. B., was a man 45 years of age. He had always been well until the present trouble started, except for a "weeping eczema" of the hands, which had recurred chiefly during the summer time, from 1893 to 1914. This had been absent since that time. The present trouble started in 1907 as dry itching spots on the elbows and shins. It had gradually progressed.

Over both elbows the skin was red, wrinkled and atrophic. The legs and the lower half of the thighs were covered with a reddened, somewhat thickened skin. In some areas there was slight lichenification and numerous excoriations due to scratching. In some areas, especially on the thighs, at the upper and outer borders of the eruption, there were elevated, urticaria-like spots. Such spots appeared, according to the statement of the patient, every three or four weeks. Their appearance was usually preceded by a short period of malaise with slight elevation of temperature. After about a week they usually disappeared, as did the intense pruritus with which they were attended.

The patient had been seen once only, and it had been impossible to complete the necessary examinations in time for presentation, but the results of these examinations would be stated later.

DISCUSSION

DR. WISE was of the opinion that the lesions were not those of mycosis fungoides, or leukemia cutis, or lymphogranulomatosis cutis, or any of the diseases grouped under the leukemias. He believed the condition more likely to be an atypical form of atrophoderma.

DR. PORTER did not care to make a diagnosis before studying the case carefully.

DR. WINFIELD said that from the imperfect examination, he was inclined to consider the case one of mycosis fungoides. The intense itching, the adenopathy and the tumefaction of some of the lesions, all pointed to that diagnosis.

DR. TRIMBLE said that it was difficult to foresee how these chronic conditions would develop. They not infrequently became transformed into other conditions after continuing from year to year. Just now the condition resembled mycosis fungoides more than any other condition, but if it was not that, it was one of those skin conditions associated with leukemia. The amount of infiltration would lead one away from the diagnosis of idiopathic atrophy. The only lesion on the patient he could reconcile with that diagnosis was the one on the elbow; there was a crinkled condition there that looked as though it might thin out and be termed cigaret-paper skin.

DR. HIGHMAN said that from the fact that the lesions were mainly on the lower half of the body, as well as the itching, the infiltration, the color and the general adenopathy, one would expect the condition to be either mycosis fungoides or leukemia. He was inclined to think it more likely to be leukemia than mycosis fungoides, but this would be revealed only by further study. He would not be surprised at the atrophy in either of these two conditions, as Dr. Wise had himself described it. The dermatoses do sometimes lead to atrophy of the skin, and there seemed to be little doubt that the case belonged to this group.

DR. MACKEE expressed the opinion that the case was either mycosis fungoides or leukemia, for the reasons already stated by the previous speakers.

DR. WISE inquired how long the condition had lasted, and on being told that the duration was six years, he asked whether one could have a leukemia for six years and show no serious constitutional changes.

ALOPECIA AREATA TOTALIS. Presented by DR. WISE for DR. FORDYCE.

A boy, aged 3, exhibited a total loss of hair, including that of the eyebrows, eyelashes and scalp. The duration of the condition was two years. The intention was to present the father and son, both of whom presented total alopecia.

DERMATITIS FACTITIA. Presented by DR. HOWARD FOX.

N. McD., a girl, 23 years of age, born in the United States, who had been employed at different times as a domestic and as a factory worker, whose family history, as far as obtainable, was negative, as a child had been operated on for a cleft palate. She was a poor student, and had left school at an early age. She had suffered from two attacks of appendicitis and from frequent colds. She had always been very nervous, and had recently suffered from "bladder trouble," occasionally requiring to be catheterized. The menses were established at 15, and had since been very irregular, the flow being slight and the pain severe.

During the past six years she had suffered from a long and varied list of accidents, each of which, according to her statement, resulted in the deforming scars which she presented. There was one deep, sharply circumscribed ulceration on the wrist and numerous scars on the forearms and other parts of the body accessible to the hands. They varied in size and shape, many of them having a distinctly artificial appearance. They were entirely too extensive and deforming to have been the result of ordinary trauma. The accidents which she recounted in detail as the cause of the individual lesions were trivial in many cases, such as a scratch, mosquito bite, venesection, slipping on a stone while bathing, etc. There was invariably an interval of several weeks between the trauma and resulting ulceration which appeared suddenly and required from one to six months to heal. There was complete absence of the corneal reflex and other stigmas of hysteria.

The diagnosis was accepted without dissent.

DISCUSSION

DR. MACKEE said that these cases are always exceedingly interesting, and one cannot see too many of them. He then cited the case of a girl who, after an appendectomy, left the hospital with the wound doing very well, but it ceased to heal and became keloidal, and was then treated with the roentgen rays. The keloid disappeared, but the wound opened again and refused to heal. It turned out to be a case of dermatitis factitia. She kept digging in the wound, and after a sealed dressing was used she stained the gauze with menstrual discharge. The number of artifices she used to fool the physician was remarkable. The wound healed with a plaster dressing. Every time the dressing was not used the wound would open.

DR. WINFIELD said he had been interested in the ulcerations, and the various things that are used by these patients to keep the wounds open. He thought the agent used in this case was caustic soda. There was always necrotic tissue when phenol was used. Caustic soda made a clean cut ulceration.

DR. HOWARD FOX said he had not attempted to induce the patient to tell the means that she had used in her self-mutilation. As malingering had been suspected, her physician had put a plaster cast on the arm. It was removed at her request at the end of three weeks as she complained of severe pain. Deep ulcerations were found at both upper and lower ends of the cast, but none on the parts that had not been accessible to her hands.

FOR DIAGNOSIS. Presented by DR. TRIMBLE for DR. ROTHWELL.

A white woman, German, 49 years old, presented a circinate arrangement of small, soft nodules, one-sixteenth or one-eighth inch in diameter, about the

tip of the nose, with small spots of superficial scarring evident in the area of the patch which had a diameter of about one-half inch. The color of these nodules was reddish-yellow or brownish-red, suggestive of the apple-jelly color of lupus nodules, and they were about six or eight in number.

The history given was that the condition was of about seven years' duration altogether, disappearing after courses of injection of mercury and mouth administration of potassium iodid, and reappearing some time after the discontinuance of such treatment. Various Wassermann reactions were negative; none was positive. There was no history of a syphilitic nature. Another blood specimen was taken four days before presentation, but the report had not yet been received.

DISCUSSION

DR. WHITEHOUSE said he had not observed the patient as long as had Dr. Trimble, so it was not quite fair to criticize the diagnosis, but from what he had seen he rather favored the diagnosis of syphilis—from the scars that remained and the circinate group of papules. Of course the mere statement by the patient that it disappeared under medication would not influence him, but the appearance of the scars bore out what the patient said about their disappearing and recurring during a period of seven years, and all this was in favor of syphilis. He did not know that lupus disappeared and recurred, but syphilis could do so in one circumscribed locality like this.

DR. HIGHMAN said that Dr. Whitehouse had expressed his views.

DR. HOWARD FOX thought the diagnosis of syphilis more probable, as the patient presented a group of dull colored nodules arranged in a circle and situated largely on one side of the nose. He thought the age of the patient also favored this diagnosis.

DR. LANE said that if the history given by the patient was correct, the condition had existed for seven years; it would seem that if it were lupus there would be no question about the diagnosis by this time; accordingly, he favored the diagnosis of syphilis.

DR. POTTER also agreed with the diagnosis of syphilis.

DR. WINFIELD expressed the opinion that the fact that the condition was relieved by medication strengthened the diagnosis of syphilis. The patient had probably been taking potassium iodid, and such lesions sometimes yield readily under that treatment. The scarring and the circinate eruption all pointed strongly to syphilis.

DR. MACKEE said that he was surprised at the unanimity of opinion expressed about a duration of seven years being common for syphilis. It had not been his experience to see syphilis recur in a restricted area for over seven years. He agreed with the diagnosis of syphilis, but was surprised at the opinions expressed. He had never seen such a case.

DR. HIGHMAN, referring to Dr. MacKee's remarks, said that Jadassohn used to point out a circinate seborrheal type of nodular or papular syphiloderm that occurred in the nasolabial fold near the tip of the nose in late secondary or early tertiary syphilis. This case seemed to meet that description. It was peculiar to people with facial seborrhea.

DR. TRIMBLE said that he had seen the case only once several days before, and at the time there was some discussion in regard to these two diagnoses, so it seemed an interesting case for presentation. He had not heard the result of the Wassermann report. The only thing that surprised him was the

unanimous opinion that the condition was syphilis. He had expected that some would consider it lupus. At first glance the lesions strongly resembled those of syphilis, though after the history had been taken, and after thinking it over carefully, it seemed to him that it was a group of lupus papules. Some one had referred to the age of the patient. It seemed that all the members were taking the woman's history into too great consideration, where as a general rule little importance was given to the history of the case. The woman did say that the lesions disappeared entirely on one or two occasions after taking some internal medication. Patients, however, often say that when the lesion does not disappear entirely, but only improves. Nor should the age of the patient be given too much consideration. He thought we must change our opinion about its always beginning in the young. Cases are seen following the tuberculosis ulcerations that occur at the mucocutaneous outlets of the body; this condition after it encroaches on the glabrous skin at times changes into lupus vulgaris.

DR. TRIMBLE said that he would report the Wassermann reaction and the result of the therapeutic test at the next meeting.

DARIER-ROUSSY SARCOID. Presented by DR. WISE for DR. FORDYCE.

S. E., an Irish housewife, 35 years of age, presented two subcutaneous nodules just above the right knee, violaceous in color. The first, of one year's duration, was the size of a large walnut and situated anteriorly. The second, which was said to be of only a week's duration, was pea-sized and located laterally. There was no tenderness. Treatment with Fowler's solution had just been started.

DISCUSSION

A number of the members expressed their agreement with the diagnosis.

DR. HIGHMAN said that he agreed with the diagnosis clinically, and had also seen a slide which confirmed it.

ARSENICAL KERATOSIS AND PIGMENTATION. Presented by DR. WISE for DR. FORDYCE.

I. W., a Russian girl, aged 20, had had chorea for twelve years, and had been taking arsenic off and on during that time. She presented extensive arsenical keratosis of the palms and soles, with pigmentation; also mottled brownish discoloration about the neck. These effects were said to be of three years' duration.

FOR DIAGNOSIS. Presented by DR. TRIMBLE for DR. ROTHWELL.

An Italian, 45 years of age, presented plaques of nodular infiltration covering most of the dorsum of one hand, including backs of phalanges (proximal) and small areas over the thenar eminence of the other palm, the color of the infiltration on the dorsum of one hand being darker than his normal pigment. On the abdomen and thighs were scattered from ten to twenty brownish-red nodules of various outlines, some giving the impression of rings, the borders being thicker than the centers. On the dorsa of the feet were purplish pigments, well defined at the border, and without apparent infiltration.

History was of about one year's duration, and except for itching of areas of pigmentation on the feet there were no subjective symptoms. He was the father of five healthy children; his wife had had no miscarriages. He denied

any knowledge of having had syphilis, and his Wassermann reaction was negative. A biopsy was made, but the report had not yet been received.

DISCUSSION

DR. TRIMBLE said that the man was one of Dr. Rothwell's private patients, and he was very undecided about the diagnosis, and had brought him to the clinic for a biopsy. The two conditions considered were Kaposi's hemorrhagic sarcoma and lepra. The biopsy report had not yet been received, but it seemed to be an unusual case. The lesions on the body and those on the face and hands seemed quite different. The condition on the feet and hands resembled Kaposi's hemorrhagic sarcoma, though there were no nodules. He was inclined to consider it a case of Kaposi's sarcoma.

DR. HIGHMAN said that it was difficult to size up such a case at a glance without a detailed study, but the major clinical features undoubtedly suggested Kaposi's sarcoma.

DRS. MACKEE, HOWARD FOX and WISE agreed with DR. HIGHMAN.

DR. WHITEHOUSE also agreed with Dr. Highman that the case clinically suggested Kaposi's sarcoma. He then inquired about the lesions on the feet and hands, and said that he had thought the history was a little longer than stated by the preceding speaker. The infiltration and the pigmentation certainly suggested Kaposi's sarcoma.

DR. TRIMBLE agreed with the diagnosis of Kaposi's sarcoma, and said that he considered it Kaposi's sarcoma when he first saw the case. This diagnosis was based on the bluish areas of the hands and feet; the lesions on the body did not seem to resemble those of Kaposi's sarcoma. He promised to report the pathology of the case at the next meeting.

DR. WINFIELD said that he had had a case of Kaposi's sarcoma under observation for many years, and at times the patient had these blue discolored spots on the body, which sometimes disappeared without treatment. He expressed the opinion that these lesions would not argue against the diagnosis of Kaposi's sarcoma.

LICHENOID PAPULAR SYPHILODERM. Presented by DR. WISE for DR. FORDYCE.

G. B., a clerk, aged 29 years, had come under observation two days previously, when a blood test was made, the report of which had not yet been received. He stated that the previous Wassermann test was positive. When first seen the patient exhibited a rash having the appearance of lichen planus, pea-sized isolated flat papules being scattered diffusely over the trunk and the inner surface of the thighs. On presentation, however, the resemblance to lichen planus was remote. The man gave a history of being married and of having had no extramarital intercourse, and no sign of any chancre on any part of the body; but stated that a maid in the house had been taken to the hospital on a stretcher with a generalized rash, the nature of which he did not know.

Diagnosis accepted without question.

UNILATERAL VASCULAR NEVUS. Presented by DR. HOWARD FOX.

V. S., a school boy, 14 years of age, born in the United States, presented an extensive "port wine" nevus of the upper and lower extremities of the

right side. The patches varied in size and shape, being darkest on the most dependent parts. On the lower extremity they extended from the sole to within a short distance of the anterior superior spine. On the upper extremity they were present on the palm, the back of the hand and the forearm. His hand was being treated by the Kromayer lamp (with pressure).

SYPHILIS OR LICHEN PLANUS? Presented by DR. HOWARD FOX.

A man, 30 years of age, referred by the U. S. Public Health Service, had been infected with syphilis two years previously while in the military service. His Wassermann reaction was said to have been positive at the time of infection. He had been treated by seven injections of arsphenamin and forty intramuscular injections of mercury, and his Wassermann reaction had been twice negative during the past year. Four weeks ago he noticed for the first time an eruption on the glans penis. This consisted of a half dozen pinhead sized, flat, dull colored papules, several of them presenting a central depression. There was no itching or other subjective symptom. He had not recently received any antisyphilitic or other treatment. He was presented for differential diagnosis between localized lichen planus and late secondary syphilis.

DISCUSSION

DR. MACKEE said that one could not differentiate clinically between the two conditions, but would have to depend on the therapeutic test and the Wassermann reaction.

TABES DORSALIS WITH CHARCOT JOINT (?). Presented by DR. HOWARD FOX.

A man, 54 years of age, referred by the U. S. Public Health Service, had suffered from a penile lesion twenty-seven years ago, though he gave no history of secondary manifestations. He had been treated with pills for about two months. The lesions of the toes were first noticed fourteen years ago, beginning as "corns" followed by ulceration of the great and second toes of the right foot. The left great toe had been amputated five years ago. During the past four months he had suffered from a swelling of the left knee joint, which was at times painful, though not tender to the touch. This had appeared without any preceding traumatism. He gave a history of bladder disturbance, lightning pains and loss of sexual power. He presented an Argyll Robertson pupil, Romberg symptoms and absence of knee jerks. Radiograms made by Dr. Foster showed: "Loss of the outer distal portion of the terminal phalanx of the left foot. Right foot shows loss of phalanges and distal half of metatarsal bone of great toe and phalanges of second toe and metatarsal bone of small toe. Lower end of femur shows erosion of outer condyle of lower end of femur." The blood Wassermann test was +. Examination of the spinal fluid (made at the Marine Hospital) showed normal findings, the cell count being 6 and the Wassermann reaction, globulin and gold curve being negative.

There were no macules suggestive of maculoanesthetic leprosy to be seen on any part of the body. The ulnar nerves appeared to be slightly enlarged, though not tender.

The patient appeared to be in good general health, with fairly strong muscles, and was well nourished. A neurologic examination by Dr. Charles A. McKendree was made subsequent to the presentation of the patient. His report was:

"Considerable swelling and deformity of the left knee. Great toes of each foot removed. Cyanosis of both feet. No special atrophy. Sphincter control is disturbed. Sexual power absent twelve years. Marked Rombergism. No ataxia of the upper extremities. No dysadiadokokinesis. The vibratory senses in the legs and arms are preserved. Position sense is markedly disturbed in the toes. Touch is preserved all over the body, except for diminished sensation on the outer side of the left leg and over the dorsum of the foot. Pin prick corresponds; warm and cool stimuli correctly interpreted, except for possibly some delay, but specially affected on the outer surface of the left leg. Reflexes of the upper extremities are present and equal. Patellar and Achilles' jerks are absent on both sides. Pupils are about equal. The left is slightly irregular; convergence reaction present; light reaction absent. Right fundus shows several extensive scars, the disk is not well made out. The left fundus shows a small scar over the disk. The disk appears fairly normal.

"Diagnosis: Neurosyphilis of tabetic type. Charcot joint."

DISCUSSION

DR. FOSTER showed a plate made in the afternoon, and expressed his regret that he had not been able to find one taken three years ago. There had been some changes in the phalanges since the patient was last seen. In the left foot there was destruction of the two terminal phalanges and part of the proximal phalanx of the great toe. The knee showed some erosion of the condyles, but there was nothing characteristic of sarcoma, which was the tentative diagnosis when under observation at the dispensary. The laboratory examination was all against the diagnosis of syphilis; the blood Wassermann reaction was +. The patient was born in Austria, near Trieste, but had visited all parts of the world and had had relations with women in every country where he had wandered practically all his life. He gave a history of venereal ulcer twenty-seven years ago, but no history of secondary infections.

DR. WHITEHOUSE said that the patient presented more symptoms of leprosy than of any other condition. Two out of five cases of lepra give a + Wassermann reaction. Dr. Whitehouse said he did not think the changes shown conformed to syphilis and was inclined to consider it a case of leprosy. He had seen patients, one from the West Indies, with both syphilis and leprosy—deforming leprosy of the hands, toes and fingers, and blindness, together with active lesions of syphilis. They had the changes of leprosy and frank syphilis at the same time.

DR. HIGHMAN said that the patient stated he was born in Istria and had gone to Melita, where a disease prevailed which is related to syringomyelia or is identical with it. The + Wassermann reaction might go with either syphilis or lepra, but was too weak to be significant. Nevertheless, the patient had Romberg's sign, Argyll Robertson pupils, Charcot's knee, etc. There was also clinical evidence of pressure on the roots. The + Wassermann reaction could be taken for what it was worth, but in neural leprosy the Wassermann reaction was usually negative. There was nothing abnormal about the ulnar nerve of this man, so the evidence favored syphilis rather than leprosy. On the other hand, the mutilation of the toes was against syphilis and somewhat favored leprosy, but not more so than syringomyelia; though whether that condition was accompanied by the disturbances which the man showed, he could not recall. On the whole, he was more inclined to the diagnosis of syringomyelia than any other condition.

DR. LANE thought that a positive diagnosis in this case could not be made on the basis of the data presented. The bone changes and the deformities of the feet could easily be attributed to leprosy, and it was possible that the changes in the bones of the knee joint also might be attributed to it. The Romberg symptom, which was slight, might be accounted for by the condition of the knee joint without the necessity of explaining it by involvement of the central nervous symptom. It was possible that both syphilis and leprosy were present. Further examination should settle this question, and should also determine whether the condition was leprosy or syringomyelia.

DR. POTTER favored the diagnosis of leprosy rather than syphilis.

DR. GEORGE H. FOX expressed his regret that he had not been able to make a careful examination of the case, but doubted that it was leprosy. In leprosy there may be ulceration and loss of the phalanges, but he did not know that it ever produced the osseous atrophy seen in this case. He was inclined to agree with Dr. Highman's suggestion that it was some other disease than either leprosy or syphilis.

DR. WISE said that Dr. Highman's suggestion had appealed to him also. If the man had enough leprosy to develop the deformity of the feet as shown, he would also show other conditions which would be recognized at a glance. It would be well to study the case along the line of Dr. Highman's suggestion.

DR. WINFIELD was inclined to agree with Dr. Highman's diagnosis. He had seen some cases of Morvan's disease in which there were the same changes in the osseous tissues. The lightning pains did go with Morvan's disease—also with leprosy and with syphilis. In his opinion the diagnosis of Morvan's disease was more likely than either syphilis or leprosy.

DR. HOWARD FOX regretted that he had only the opportunity of making one brief examination of the patient. He did not think the case one of leprosy. With such marked changes in the toes in leprosy we would expect to find other changes, such as anesthesia, pigmentation, enlarged ulnar nerves, etc. The diagnosis of anesthetic leprosy might be settled by microscopic examination of the nasal mucous membrane. As the patient presented an Argyll Robertson pupil, loss of knee jerks, a possible Charcot's joint, and complaint of lightning pains and bladder disturbances, a probable diagnosis of tabes had been made. The changes in the toes, however, did not seem to accord with this diagnosis, which he thought was also weakened by the negative Wassermann findings in the spinal fluid. The idea of Morvan's disease had not occurred to the presenter.

DR. FOSTER said that three years ago, when he first saw the patient, he had thought of leprosy and syphilis, but the changes in the bones of the feet, as shown by the roentgen ray, pointed against syphilis; there was no bone production, and with a + Wassermann reaction, a negative spinal fluid, and a cell count of 6, it did not seem to be syphilis. The man was a sailor, and had been exposed to both diseases in his travels all over the world.

DR. FOSTER said that he had entirely overlooked the possibility of Morvan's disease, and it had never occurred to him until suggested by Dr. Highman. In his mind it had been a question of diagnosis between syphilis and leprosy, and he had submitted the case for an opinion on the matter.

CASES PREVIOUSLY PRESENTED.

DR. HIGHMAN said he wished to report on the case of lichen hypertrophicus. Histologically the diagnosis was confirmed. After a roentgen-ray examina-

tion a marked involution of the lesions took place, and he hoped to be able to report more later.

DR. WINFIELD said that he had recently seen an interesting case of syphilis and Vincent's angina occurring simultaneously. The patient was taken ill six weeks ago with temperature and sore throat and a membrane. The attending physician diagnosed the case as diphtheria and sent a culture to the board of health. The report came back negative. A culture was also sent to a private laboratory, and they reported Vincent's angina. The throat symptom cleared up under treatment, but the man did not get well; so he was examined further and a +++ Wassermann reaction was obtained. He then said that during the summer he had a pimple on the shaft of the penis. No eruption followed, and his throat is now practically well.

DR. HIGHMAN said that in the army he saw several cases of so-called Vincent's angina, and discussing the matter with laboratory workers, he got the impression that the organisms of that disease were not of established pathogenicity. In one instance a gumma of the tongue showed the organism of Vincent's angina; the patient was treated with arsphenamin and the lesion healed. But a buccal gumma might show these organisms if they were saprophytes, and the lesions might heal with intravenous therapy. In another case there was a negative Wassermann reaction, and the local application of arsphenamin used as a dusting powder worked well. What the real truth of the pathogenesis of Vincent's angina is, he did not know.

NEW YORK ACADEMY OF MEDICINE, SECTION ON DERMATOLOGY AND SYPHILIS

Regular Meeting, Nov. 3, 1920

JOHN E. LANE, M.D., *Chairman*

EXTENSIVE VERRUCAE OF FEET. Presented by DR. TRIMBLE.

T. L., aged 36, a Porto Rican, had a negative family history. His personal history was negative. Present Condition: The lesions began on the dorsum of the left foot twenty-five years ago as small warts. The patient at that time was working barefooted in the tobacco and sugar fields of Porto Rico. The lesions gradually increased in size, and at the end of six months spread to the dorsum of the right foot. The lesions have continued to enlarge and spread until they have attained their present size. A few years ago after scratching the feet and getting blood on the fingers, the patient noticed lesions on the fingers. The eruption consisted of discrete and confluent brownish, verrucous lesions, varying in size from that of a small pea to that of a pigeon's egg, covering the feet and extending up the leg; they were also on the fingers.

Laboratory Report: The Wassermann reaction was negative. Pathologic Report: Verruca.

CUTIS VERTICIS GYRATA. Presented by DR. TRIMBLE.

A young man, aged 25, had noticed for four years some slight ridges in the anterior part of his scalp, which seemed to be deepening as the years went by. The condition at present consisted of a number of rather deep sulci

with corresponding ridges running longitudinally along the front of the scalp. The lesion apparently started about one-third the distance back from the forehead, and seemed to become more prominent as they ran forward. The patient had a good growth of hair, though it was lost in some areas in front.

DISCUSSION

DR. LEVIN said that the case which he and Dr. Wise reported showed transverse ridges and furrows over the occipital region of the scalp, and he recollected that there were distinct signs of a pituitary type of person. The cause of the condition in their case could not be determined. This condition also occurred in a patient with pituitary markings, and it is possible that further study may disclose a relation between endocrine disorder and the structural changes in the scalp.

MULTIPLE HEMORRHAGIC SARCOMA OF KAPOSÍ. Presented by
DR. TRIMBLE.

A man, aged 62, a Jew, whose family and personal history were negative, presented a condition which began six years ago on the left foot. The condition appeared as blotchy diffuse redness; two years later the redness appeared on the right foot; two and one-half years after this small tumors appeared on both feet and legs, with no accompanying symptoms, except slight edema. The tumors had not increased in size; the lesions were limited to the lower part of the legs below the knees. Both feet presented purplish brown discolorations with many tumors scattered over them, ranging in size from that of a small pea to that of a bean. The laboratory reported the Wassermann test negative. Pathologic Report: Multiple hemorrhagic sarcoma.

LICHEN RUBER ACUMINATUS. Presented by DR. TRIMBLE.

A man, aged 37, a German, whose personal history was negative, six years ago developed pruritus of the feet, which gradually spread up the legs. No eruption was noticed at this time. The patient was accustomed to rubbing the entire body with alcohol each day. January, 1920, the present trouble began. The eruption began as scaling and pruritus of the scalp. In one week the eruption spread downward, involving the entire body; it was non-pruritic except when the body was dry. The eruption consisted of reddish discrete papules; over the greater part of the body they were confluent. The papules were follicular and scaly; the palms and soles greatly thickened. The Wassermann reaction was negative.

LICHEN PLANUS (?) IN A SYPHILITIC PATIENT. Presented by
DR. WISE.

N. P., aged 28 years, single, a painter, French, had been receiving anti-syphilitic treatment at the Vanderbilt Clinic since March, 1920. The lesions in question were situated on the prepuce and glans penis and on the inner aspect of the left leg. They first appeared on the penis in January, 1920, and on the leg a month ago. On the penis were several discrete and confluent purplish papules. The lesion on the leg was the size of a quarter, of violaceous hue, and covered with fine adherent scales.

EPIDERMOLYSIS BULLOSA. Presented by DR. ROTHWELL. (From the service of Dr. Trimble.)

An Italian boy, 5 years old, presented a generalized eruption of ruptured and crusted, as well as unruptured bullae, the legs, arms and face presenting most involvement, though the trunk presented a few ruptured lesions. There was little of areola about the lesions, some being as large as a half dollar, others not larger than a ten-cent piece.

The parents stated that the condition had been present since birth, but the lesions last only a few days. Bullae could be produced by scarifying the skin and by twisting it between the fingers.

NEVO-HEMANGIO-LYMPHANGIOMA OF THE LEFT LEG. Presented by DR. ABRAMOWITZ.

Richard O'C., 15 years old, born in the United States, had had skin disease since birth. He presented himself at Dr. Fordyce's clinic, stating that for the past five years his left leg had been getting thicker. Beginning on the dorsum of the left foot were large, livid, flat patches which extended almost continuously up to the middle of the thigh. Some of these patches were covered with verrucous lymph vesicles (lymphangioma), and other patches were made up of soft cavernous angiomas. Varicose veins were also present on other parts of the leg.

ACRODERMATITIS CHRONICA ATROPHICANS. Presented by DR. ROSTENBERG.

A woman 52 years old, born in Russia, married thirty years, had never been pregnant. Her family history was irrelevant. She had always been well, but had always been easily chilled. Her present skin trouble began about four years ago with pain and swelling of the legs. She was a fairly well nourished woman. The internal organs were normal. The urine was normal and the Wassermann reaction was negative.

The skin lesion extended over both limbs and buttocks, sharply ending at the iliac crests. Anetoderma was well marked at both knees and buttocks. The skin over both tibiae and feet appeared bluish red, transparent and thinned out, the subcutaneous veins appearing most prominently in these areas. The hands and forearms were not involved.

ACRODERMATITIS CHRONICA ATROPHICANS. Presented by DR. ROSTENBERG.

Mrs. R. H., aged 40, born in Austria and for seven years resident in this country, was never sick, except for a severe burn which she sustained eighteen years ago over the same area which was involved on presentation. Her present skin trouble began, however, only three years ago, with pain and swelling of both feet, soon involving the entire legs. The legs and buttocks were involved, leaving free a sharply defined triangular area on the outer aspects of both legs. The skin over the knees showed the characteristic pigmented infiltration and marked anetoderma. The same condition was present on the buttocks. The skin over the tibiae, and especially over the dorsum of both feet, was very much atrophied and transparent, the underlying veins showing plainly. There was a small ulceration over the right outer malleolus, and another larger one over the tibial region. The hands and forearms were not involved.

NODULAR LEPROSY. Presented by DR. ROTHWELL. (From the service of Dr. Trimble.)

An Italian woman, married, 29 years of age, presented a typical leonine countenance, with some loss of eyebrow; there was a nodule on the sclerotic coat of the left eye; she had much thickened ulnar nerves; there were various areas of anesthesia on trunk. The duration of the condition was two years. She had been eighteen years in the United States.

Biopsy demonstrated the presence of Hansen's bacilli. The Wassermann reaction was + + + +. An apparent improvement was noted after a course of six intravenous arsphenamin injections.

NEVUS UNIUS LATERALIS. Presented by DR. ROTHWELL. (From the service of Dr. Trimble.)

An Italian girl, 14 years old, presented a hypertrophied, pigmented mole on the left cheek, involving the vermilion border of both lips and mucous membrane lining both lips. The cutaneous lesion on the cheek was irregular in outline, the hypertrophy being loose and pendant, and gradually narrowing to a line about one-eighth inch broad as the angle of the mouth is approached. The portion involving the vermilion border was verrucous in character.

DERMATITIS HERPETIFORMIS. Presented by DR. ROSTENBERG.

The patient, 17 years old, born in New York, came of healthy parents, and was one of eight children, of which five died in infancy. The patient claims that her present illness followed an attack of chickenpox when she was 5 years old, and that she had never been free from it since. She came under observation at the Mount Sinai Hospital in Dr. Rosen's service about three years ago, at the age of 14. With the exception of her skin trouble, she appeared to be in good health, and gave the impression physically as well as mentally of a much older woman. Menstruation began at the age of 9, and she claimed to have been fully developed at that time.

She presented a large number of areas all over her body, which resembled an acute weeping eczema, and a tentative diagnosis of infectious dermatitis was made. Endocrine disturbance was suspected, and she was given thyroid in addition to ointment. The improvement was slight and not lasting; one attack would follow the other, and on account of the grouping of the lesions and the extreme itching, the diagnosis of dermatitis herpetiformis was made. A roentgen-ray picture of her head revealed a small sella turcica with bridging of the clinoid processes. Pituitary extract had as little effect as thyroid extract.

DISCUSSION

DR. ABRAMOWITZ said that the eruption had the appearances of a neurodermite. The history obtained was that the itching occurred first, followed by the appearance of papules.

DR. HIGHMAN said that he had observed the patient for a year, off and on, and that she had a dermatitis herpetiformis, although she did not show it when presented.

DR. ROSTENBERG said that the diagnosis of the condition as presented was difficult, but when the patient first came under his observation the question of infectious dermatitis came up, and finally this grouping of dermatitis herpetiformis was observed and the diagnosis was made. The condition had cleared

up and the patient was better than she had ever been, but every once in a while she has a terrific attack of dermatitis herpetiformis.

DERMATITIS EXFOLIATIVA FOLLOWING PSORIASIS. Presented by
DR. TRIMBLE.

The patient was a Jewish woman, aged 31, whose family and personal history were negative. The present illness began at the age of 14. The lesions started on the elbows and knees, finally spreading over the entire surface of the body. The eruption had cleared up several times under treatment, but it returns in from a few months to about two years. The eruption was confluent, generalized, red and scaly. There was extreme scaling in the hair.

SKIN LESIONS ASSOCIATED WITH EVIDENCES OF ENDOCRINE
DISORDER. Presented by DR. LEVIN.

Patient was presented at the March, 1920, meeting of the section.

Abstract of History.—Y. Z., a married woman, aged 38, a Russian, had had measles and typhoid in childhood. She had a pelvic operation thirteen years ago and tinea saginata one year ago. Menses began at 13 and were irregular and scanty. There was no dysmenorrhea. She had been married sixteen years; she had had five children; two were dead from accidents.

The skin condition was of seven years' duration. It began with pruritus, and after two years distinct hyperhidrosis was noticed. For two years the pruritus had been intense; the sweating had increased markedly; attacks of erythema with excessive sweating appeared now and then. A generalized increased pigmentation and oozing eczema had developed.

General symptoms had been present for two years. There were loss of weight and strength and she tired easily. She had almost constant headache (frontal); a capricious appetite, constipation, urination hourly and loss of sexual desire.

Skin Condition in March, 1919.—The skin was dry, thickened, pigmented, roughened, and covered with follicular papules. There was generalized lichenified and vesicular eczema which was most distinct on the face, neck, upper extremities and waist line. The hair was black, dry, coarse, and thinned, especially in the axillae and pubic region. Her hands were cold and moist.

Endocrine Markings.—She had had measles and typhoid in childhood. She had dry, thickened skin, dry hair, attacks of erythema and sweating, alopecia and constipation; the basal metabolism was lessened.

She was of a pituitary-skeletal-small stature with small bones, stubbed fingers, small chin, small, separated teeth, increased glucose tolerance and polyuria.

Suprarenal-increased pigmentation, low blood pressure, scoliosis with flat feet, loss of strength, increased fatigability, pigmented tumor (chin); gonad-loss of sexual desire, scanty menstrual flow, sweating and flushing were also present.

Diagnosis: Skin lesions associated with pluriglandular disorder.

TINEA OF NAILS ON THE HANDS; KERATOSES (TINEA?) OF
SOLES OF FEET. Presented by DR. WISE.

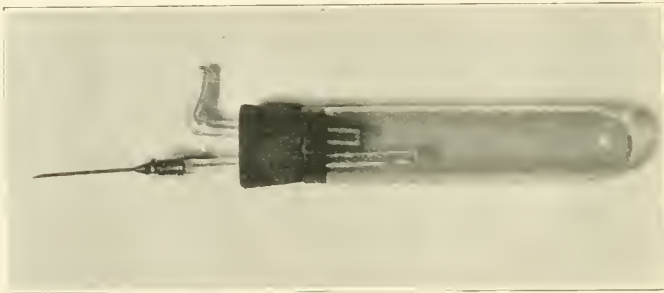
D. H., a Russian woman, aged 30 years and married, presented herself at Professor Fordyce's clinic, giving the history of trouble with her nails for one

year. The nails showed a fine stippling, some of which was arranged in transverse and longitudinal lines. The soles and heels showed keratotic brown patches, varying in size from that of a five-cent piece to that of a quarter, all of three months' duration. There were many deep rhagades in the keratotic patches, which occasionally bled.

DEMONSTRATION OF A SUBSTITUTE FOR THE McRAE NEEDLE.

DR. LANE.

Dr. Lane said that the McRae needle was an excellent device for drawing blood in cases in which aspiration was necessary for getting the desired amount. The difficulty of cleaning the needle and the inconvenience of having needles of only one size available, had led him to devise a substitute which he had found quite satisfactory. This substitute consisted of a small glass tube, ground at one end to fit a Luer needle, put through a rubber stopper, together with another glass tube for attachment to the aspirating tube. In case a small necked centrifuge tube is used, the stopper is not large enough to take both



A substitute for the McRae needle.

glass tubes, and a needle of large bore is substituted for the glass aspirating tube and an ordinary adaptor is used to connect it with the rubber tubing. This apparatus is inexpensive, easy to clean and by varying the size of the needle and stopper it may be used on any bottle and any desired amount of blood may be easily withdrawn.

Dr. Lane also demonstrated an apparatus for the alkalization of arsenophenamin solutions, a detailed description of which will shortly appear in *The Journal of the American Medical Association*.

NEW YORK ACADEMY OF MEDICINE, SECTION ON DERMATOLOGY AND SYPHILIS

Regular Meeting, Dec. 7, 1920

JOHN E. LANE, M.D., *Chairman*

GRANULOMA ANNULARE, SHOWING THE EFFECT OF ROENTGEN- RAY THERAPY. Presented by DR. CHARGIN.

Mr. K. was presented before the section in 1915, with typical lesions of granuloma annulare on the backs of the hands, fingers and ears. From that time until 1919 he had been receiving roentgen-ray treatment, having received

a total of 12 skin units. He had received no treatment of the hands during the past year, and there had been no recurrence of lesions on the hands, although he had developed a mild degree of telangiectasia at the sites of exposure. He still exhibited some of the old lesions on the ears and neck and had developed new areas of granuloma annulare on neck and cheeks.

ACTIVE SECONDARY SYPHILIS (PUSTULAR SYPHILIDS). Presented by DR. LEVIN.

T. N., an Italian, aged 27, unmarried, a diver, stated that the eruption had been present for four weeks. He left Italy just before the appearance of the eruption. The chancre appeared about eight weeks before presentation. Sore throat, headaches and falling of the hair accompanied the eruption.

The skin showed a generalized, bilateral, follicular and nonfollicular papular and pustulopapular eruption. On the face, scalp and trunk there were also several pea-sized, scaly, ham-colored papules. There was a healing chancre on the prepuce. There was an extensive alopecia of the scalp, most marked in the frontal region. He also had a generalized adenopathy, mucous patches and pharyngitis. A Wassermann test had been made, but the report had not been received.

PARAPSORIASIS. Presented by DR. CHARGIN.

E. B., a man, single, 25 years of age, a painter, had an eruption which began about ten months ago. At that time the patient presented a faint macular eruption on the back and a mixture of papules and macules on the arms, buttocks and upper part of the legs. The eruption on the back had since involuted. When presented, the eruption was limited to the arms, buttocks and outer part of the legs, and was made up of a network of macules with scattered small papules. There was likewise a faint macular eruption on the back. The papules showed a scaling which was small and white. The general color of the eruption was pale red. There was no scarring or atrophy. Subjectively, there was no itching, but there was occasional burning. The Wassermann reaction was negative.

Dr. Chargin stated that when first seen the diagnosis in this case was somewhat puzzling. The eruption on the body strongly suggested a macular syphilid, although that on the arms and buttocks looked more like seborrheic eczema. The diagnosis of syphilis was, however, ruled out by the history and the subsequent course of events. Seborrheic eczema could be excluded by the lack of involvement of the scalp and face, and the character of the scales, which were of the seborrheic type. Moreover, the liberal use of a mixed chrysarobin ointment had no influence on the eruption.

URTICARIA PIGMENTOSA. Presented by DR. WISE.

L. F., aged 42, a painter, born in the United States, presented himself at Dr. Fordyce's clinic with an eruption on the back, buttocks and axillae, which had been present about two years without any intermission. The patient complained of moderate itching. As presented, the patient exhibited numerous split-pea sized papules of an erythematous shade, which, as they faded, left a brown pigmented macule.

DISCUSSION

DR. HIGHMAN said that he had seen a section of the tissue, but on account of the difficulty in staining it he was not sure whether there were cells. The

infiltration corresponded to xanthelasmaidea, and involution was taking place in the way described by Hartzell. He said that often in this disease the mast cells could no longer be recognized during involution. Nevertheless, the general structure of the tissue indicated urticaria pigmentosa, which, considering the age of the patient when the condition began, brings up the point whether there is a form that can be called urticaria pigmentosa acquisita.

DR. ABRAMOWITZ said that the question brought up by Dr. Highman was interesting. Quinquad mentioned a number of cases acquired by adults. There had been a few patients at the Vanderbilt Clinic in which clinically the eruption seemed to be xanthelasmaidea, yet the mast cells could not be found in the section. The French called these cases *maladie pigmentie urticant*.

DR. FRASER said that we should be on our guard against calling these cases urticaria pigmentosa unless the mast cells were found in the section. As he understood it, urticaria pigmentosa was rather rare in adults. The last case that he saw so diagnosed in an adult proved to be scabies, and the patient became well under treatment for scabies.

DR. HIGHMAN said he was willing to guarantee from the clinical appearance that this was not a case of scabies. As a matter of fact, urticaria pigmentosa disappears at about the age of adolescence, the lesions leaving small brownish lentiginous spots. Unquestionably there were no mast cells in these spots. Somewhere during involution the mast cells must vanish, and for that reason Hartzell's contention seemed probable. Urticaria pigmentosa can exist as a recognizable clinical picture, yet a given lesion may not show the pathognomonic structure.

In regard to an inquiry by Dr. Lane relating to the precise clinical difference, Dr. Highman said that it was similar to that of prurigo, without many mast cells and ordinarily the finding of chronic inflammation.

DR. OULMANN said that this patient did not complain of itching at any time during the outbreak; while therefore scabies must be entirely excluded, the diagnosis of urticaria pigmentosa is doubtful. A number of years ago, Dr. Oulmann presented a case which afterward was also presented by Dr. Bechet; the condition had spread and the patient had lesions in the mouth. Dr. Oulmann's diagnosis was *xanthoma planum et elevatum*, and the condition consisted of similar brownish, slightly elevated and flat tumors. The present case was not so far advanced. The only difference was that in Dr. Oulmann's case there were lesions also over the sacral region, a place of predilection. The microscopic picture does not indicate urticaria pigmentosa. The case has to be followed up further.

DR. POLLITZER said he wished to call attention to a fact that seemed to have escaped some of the members, i. e., that this man presented urticarial wheals, not only fixed papules, but wheals that appeared on irritation.

DR. LANE asked whether there were any without irritation. That was the point.

DR. WISE said he was not certain about the last point, but thought the patient had wheals only when the skin was scratched or irritated. The speaker believed, with other observers, that a form of urticaria pigmentosa in adults occurred in which mast cells were not always demonstrable.

PEMPHIGUS VULGARIS. Presented by DR. SCHEER.

A. W., a man, aged 44 years, a subway guard, was a patient in Dr. Fordyce's clinic. The condition began three months before presentation with sore throat

and hoarseness. The hoarseness disappeared in three weeks, but he complained of sore throat. The patient presented several erosions in the mouth, the sites of ruptured vesicles; the largest of these was on the right tonsil. Irregularly scattered over the chest, back and abdomen were crusted lesions varying in size from one-eighth to three-fourths inch in diameter. These had all begun as vesicles or bullae. There were also some light-brownish pigmented spots where the crusts had fallen off. The patient was apparently in good health. He had lost 2 pounds since the onset of his illness.

MALUM PERFORANS PEDIS AND ALOPECIA OF THE THYRO-GONADAL TYPE IN A SYPHILITIC PATIENT SHOWING DEFORMITIES OF THE SELLA TURCICA. Presented by DR. LEVIN.

J. S., a married Italian, aged 41, a laborer, applied for treatment of a painful ulcer of the left foot two months ago. The family history and past history were negative for syphilis. The ulcer of the left foot appeared about two years ago and has always been painful.

The left foot showed two deep ulcers on the plantar surface. The larger was situated over the first metatarsophalangeal joint. It measured about half an inch in diameter, was round, deep, surrounded by a horny growth, and led to a sinus discharging a seropurulent fluid. The second ulcer on the third metatarsophalangeal joint was smaller and not so deep. The plantar surface of the right foot showed hyperkeratotic patches over the metatarsophalangeal joints with beginning ulcers. The skin of both legs in front and in the region of the knees showed large, pigmented, cigaret-paper-like scars. There were hyperhidrosis and bromidrosis of the feet.

The skin of the rest of the body was white, soft and of fine texture and resembled that of a female. The hair of the eyebrows and eyelashes was missing. The mustache region and beard showed patches of baldness, and the rest of the hair was thinned out. Both axillae showed a sparse growth, and the pubic hair was of the female type. The forehead was wide; the frontal bosses, the glabella and the superciliary ridges were prominent. There was a marked separation of the incisor teeth. The pelvis was of the female type, and the voice also was feminine in character. The Wassermann reaction of the blood was +.

A radiogram of the skull showed a small, shallow, deformed sella turcica, and the anterior clinoid process was enlarged and deformed.

DISCUSSION

DR. LEVIN stated that he had presented the case to show the peculiar alopecia present in the patient, rather than the perforating ulcers. The patient had syphilis and showed the markings of a pituitary type of person. He showed an absence of the eyebrows and eyelashes. There was alopecia of the beard and mustache; the axillary hairs were very much thinned out, and the pubic hair was of the female type.

According to Leopold-Levi, the growth of the eyebrows and eyelashes is controlled by the thyroid gland; the growth of the axillary hairs and the pubic hairs is controlled directly by the gonads, and the pituitary gland acts only indirectly through the gonads on the growth of hair. This person therefore is a pituitary type with thyrogonadal alopecia, according to the findings of Leopold-Levi.

Dr. LeWald said that he would like to see the roentgenogram. Recently he had spent an afternoon in a Boston clinic studying pituitary fossa variations, and they were quite at sea there in regard to the normal pituitary fossa; there are so many variations in the supposedly normal person that one has to be very cautious in expressing an opinion as to the function of the pituitary gland from an inference of the so-called abnormal form of the pituitary fossa or over-riding clinoid processes. One would find extreme variations in 100 persons. Dr. E. W. Caldwell examined the frontal sinuses of 100 persons; he found such extreme variations that unless there is great erosion or great enlargement, such as is seen at times, one must be very cautious in drawing a conclusion from a mere prominence of the clinoid processes and apparent smallness of the fossa.

Dr. LEVIN said the report on the radiographic findings in this case was that obtained from the roentgen-ray department of the Cornell University Medical College and Clinic. Those of us who do not specialize in this branch of medicine must accept the reports of the experienced worker. Of course, we recognize the fact that it is yet impossible to state positively what constitutes a normal sella turcica as seen with the roentgen ray.

ORIENTAL SORE. Presented by Dr. CHARGIN.

C. L., a man, aged 19, single, a tailor, a native of Turkey, who had been in the United States about four months, had a lesion of eight months' duration, which began as a small sore that gradually increased in size until it became as large as a five-cent piece. During the last two months it had been undergoing involution. The lesion was located on the lower lip at the left corner of the mouth, on the vermilion surface, and was the size of a ten-cent piece when presented. It was somewhat hard and covered with a crust, the removal of which disclosed an irregular ulcerated base. There was a moderate amount of submaxillary adenitis. Smears for spirochetes and for Leishman bodies were negative. The Wassermann reaction was negative. The patient had received three intravenous arsphenamin injections.

DISCUSSION

Dr. CHARGIN stated that the first impression gained was that the lesion was a chancre, but this theory had to be discarded when numerous examinations for spirochetes proved negative. Moreover, there was absence of a marked submaxillary adenitis; the Wassermann reaction was negative; and there was absence of either a history or evidence of a secondary eruption. Gumma was ruled out by the absence of syphilitic history, a negative Wassermann reaction, consistency of the tumor, the presence of adenitis, and lastly by the course of the condition. Epithelioma was likewise considered. This diagnosis was improbable on account of the youth of the patient; also the glandular enlargement was not sufficient in amount; and that which was most important was the fact that the lesion showed definite involution which seemed to exclude epithelioma. With the knowledge that he recently arrived from the Orient, oriental sore came to mind, and although we have thus far not been able to demonstrate the Leishman bodies, the diagnosis of oriental sore seems justified both by exclusion and from clinical findings.

Dr. MacKEE said he could not question the diagnosis because he had never seen an oriental sore; he hoped this would prove to be a case so that we could profit by the experience. He had, however, been wondering whether the pos-

sibility of tuberculosis had been considered. Clinically the lesion was of the character that suggested that possibility, although the enlargement of the glands of the neck did not occur so often in tuberculosis.

DR. HIGHMAN said that his knowledge of the oriental sore was about equal to what he knew of the ductless glands, only he would like to caution Dr. Chargin against ruling out epithelioma on account of the youth of the patient. That was rather dangerous, as he had seen epithelioma in a girl of 17.

DR. POLLITZER said he had been impressed with the word ulceration in Dr. Chargin's presentation. Was the lesion an ulcer when he first saw it?

DR. CHARGIN, replying to Dr. Pollitzer, said that the lesion was covered with a crust, the removal of which revealed an irregular ulcerating sore.

DR. POLLITZER said that the evidence was in favor of the diagnosis submitted, though it was based chiefly on exclusion. It was an easy matter to rule out the various possibilities mentioned; but the fact that the lesion resembled an involuting Aleppo boil, and that the man came from the Aleppo boil region, together with the negative evidence, seemed to be sufficient reason for accepting that diagnosis as probable.

DR. WILLIAMS said it was a very interesting case. At first sight it suggested the primary lesion of syphilis, but on careful examination that could be ruled out. It was impossible to exclude Aleppo boil, and that was the probable diagnosis. The boy, however, had the habit of licking the side of the mouth and keeping it constantly wet with saliva, and it was possible that it was an ordinary granuloma kept irritated by constant licking and wetting.

DR. HOWARD FOX said that he had recently had the opportunity of studying a case of oriental sore at Ellis Island. In this case the lesions were all situated on the face, following the general rule of being present on the exposed parts. While most authorities stated that the eruption generally consisted of a single or at least few elements, in his case there were ten distinct lesions. The diagnosis had been confirmed by finding the Leishman-Donovan bodies in the sections. According to the experience of others, the clinical diagnosis was often difficult. Castellani and Chalmers stated that there were six distinct clinical types. In some cases the differential diagnosis between syphilis, tuberculosis and blastomycosis was difficult, and could only be definitely settled by finding the organism in smears or sections.

DR. SATENSTEIN said that he had had opportunity to study sixty-two or sixty-three cases, some from Damascus, some from Aleppo and some from Turkey. Two types were found—one from Turkey, and the other (the breaking down type) from Damascus and Aleppo. The lesions always appeared on the exposed parts of the body. In all the cases he saw only two had single lesions, one of them on the nose of a boy of 5, and the other on the cheek of the patient. All the other cases were multiple, one of them having eighty or ninety lesions. A Wassermann test was made before, during and after treatment. Practically every case responded to arsphenamin, but not to arsphenamin as given here—once a week—but three times a week together with local treatment. Some of the eruptions involuted as a result of ordinary cleanliness without treatment. In from four to six weeks the lesions disappear, and they appear only on the exposed parts. Dr. Chargin mentioned that his patient was receiving arsphenamin. The lesion had the pearly border and the softness that corresponded to many of the cases seen. As for the microscopic examination, Dr. Satenstein said they had never accepted a case of oriental sore unless the organisms were found. They always made an incision at the

margin of the lesion, curetted some of the tissue, and looked for the living organisms. He could not recall that a successful smear had been made at any time. The organism was found in the tissues and in the fresh preparations, but never in a stained smear.

DR. HIGHMAN inquired how rapidly the cases responded to arsphenamin.

DR. SATENSTEIN replied that six weeks was the shortest time required.

DR. CHARGIN said that the textbook descriptions usually state that the organisms are found in the scrapings and smears made from the blood obtained from the sores. The fact that the organism was not demonstrated in this case may be accounted for by the fact that the lesion was involuting, and it is a known fact that as the sores get better the organisms tend to disappear. The patient had improved 50 per cent. since he was first observed, and it was doubtful as to whether the organism could now be found.

DR. HIGHMAN suggested the use of Romanowsky stain.

DR. CHARGIN said he had used the Wright, Giemsa, as well as the Romanowsky, stain.

LUPUS ERYTHEMATOSUS? Presented by DR. ABRAMOWITZ.

A. M., 46 years old, a Russian, street cleaner, presented himself at Dr. Fordyce's clinic with an eruption confined to the scalp, cheeks, nose and ears, of fifteen years' duration. The patient exhibited an eruption of the regions mentioned consisting of well-defined erythematous lesions covered with fine white scales, and atrophy. He also showed destruction of the helix of the ears and ectropion. No subjective symptoms were present.

DISCUSSION

DR. WILLIAMS said that the scalp presented the typical picture of lupus erythematosus, whereas the appearance of the nose was typical of lupus vulgaris; the border with the brown pigmentation looked like lupus vulgaris; there were definite ulcerations on the ear and face; and the man gave a history of having frequent ulcerations, which was not characteristic of lupus erythematosus but of lupus vulgaris. It was possibly a case of both lupus erythematosus and lupus vulgaris. He had lupus erythematosus and probably lupus vulgaris also.

DR. POLLITZER said the man had lupus vulgaris so far as the lesions of the face were concerned. Lupus erythematosus did not produce that amount of destruction. The upper part of the right ear was damaged to an extent never caused by lupus erythematosus. He had been surprised to hear that the diagnosis of lupus erythematosus had been made. It impressed him as a typical case of extensive old lupus vulgaris of the face. On the scalp the condition resembled lupus erythematosus, and it was possible that there was a combination of the two.

DR. HOWARD FOX felt that a case of this type could be indefinitely discussed without arriving at any unanimity of opinion. Some would consider it lupus vulgaris and others lupus erythematosus. He thought the question might be settled by the microscope. His personal opinion was that clinically the disease was lupus erythematosus. He thought that the entire eruption was either one disease or the other and did not like to straddle the question by suggesting that one part of the eruption was lupus vulgaris and another lupus erythematosus. The number of cases of the two diseases occurring simultaneously in the same person was extremely small.

DR. LANE asked whether the microscopic diagnosis of the lesions on the face could settle the question if no apple jelly nodules were found.

DR. GILMOUR suggested that a microscopic diagnosis should be made and the result reported at the next meeting.

DR. LEVIN said that the question in his mind was whether the deformity resulted from destruction of tissue or whether it resulted from pressure of tense or shrinking skin covering hard tissue like the cartilage of the nose and ears, as in this case. He regarded this as a case of lupus erythematosus.

DR. HIGHMAN said he had not seen the case, but in connection with the microscopic study of these lesions, he wished to caution against placing too much faith in the microscope. To do the work properly one would have to take specimens from two different areas and study them; the microscopic structure of lupus erythematosus was not always convincing, as was that of lupus vulgaris, but if negative evidence were found in a specimen from the scalp one could not be positive that he was not dealing with an inflammatory process near the lupus vulgaris lesion that had nothing to do with the tuberculous tissue itself. One case of the combination of lupus vulgaris and lupus erythematosus was published in the *Archiv für Dermatologie*, January, 1909.

URTICARIA PIGMENTOSA. Presented by DR. ABRAMOWITZ.

J. T., 5 months old, of Italian parentage, was brought to Dr. Fordyce's clinic with the history that the eruption had been present for four months. The lesions were numerous on the back and extremities, and were split-pea or almond sized, of a yellowish-brown color and showed urtication on friction.

A biopsy revealed the usual structure of urticaria pigmentosa, with mast cell infiltration.

SYPHILOMA VULVAE. Presented by DR. LEVIN.

A young woman of 20, was first shown in May, 1919. She stated that for the last six months she had noticed a large swelling, growing larger and larger. She said that she had no pain and no discomfort, and her general condition was in no way influenced by the growth. The present picture was somewhat different from that when she was first seen, when there was one hard parchment-like pendulous tumor hanging down between the thighs, the size of a child's fist, originating in the labium. Where the tumor touched the labia majora there were ulcerations. The blood examination on two different occasions gave a +++ and ++++ Wassermann reaction. Dr. Fox was asked to look at the patient, and he too made a clinical diagnosis of syphiloma—a tertiary manifestation of syphilis. The procedure at that time was to excise all of the affected area, which was done without any trouble, and at the same time to give the patient intense antisyphilitic treatment—intramuscular injections twice weekly. She left the hospital earlier than was thought wise, and half a year later came back with a similar condition; she was again operated on and again left the hospital earlier than advised; she then came back and received antisyphilitic treatment, and for the first time the Wassermann reaction was negative. The patient was presented for suggestions as to treatment.

DISCUSSION

DR. MACKEE said that he did not feel capable of discussing the subject he was about to broach, for he had never seen any of these cases; but he would think seriously of ulcerating granuloma. Dr. Goodman, who had seen some cases in Porto Rico, might say a few words in regard to it.

DR. GOODMAN said that the case resembled clinically the cases of ulcerating granuloma which he had seen in the tropics. The character of ulcerations with cicatrization and the hypertrophy through which hairs appeared were suggestive. The invasion of the vagina and the beginning ulceration of the anterior border of the anus were such that he was inclined to think that ulcerating granuloma was the condition presented. Bacteriologic studies would disclose either the *Calimato bacterium granulomatis* of Donovan, or the *Spirochaeta aboriginalis* of Wise. The biopsy would also aid in the diagnosis. He had reported his cases in full soon after his two years' tour of duty in the tropics.¹

DR. HIGHMAN said that among other things to be considered was the possibility of the patient having a cicatrization following syphilis, with local elephantiasis.

DR. STEIN asked what therapy Dr. Goodman would suggest.

DR. GOODMAN advised antimony and potassium tartrate (tartar emetic) given in 1 per cent. solution intravenously. Five c.c. may be given every other day; if 5 c.c. are diluted to 25 c.c., the pains along the arm of which the patient may complain are avoided.

HODGKIN'S DISEASE OF THE SKIN. Presented by DR. WISE.

M. G., 21 years of age, born in the United States, married, no children, presented herself at Professor Fordyce's clinic about ten days previously, complaining that about two years ago she began to have some itching. This was followed by swollen glands and the appearance of an eruption all over the body except the face, scalp and legs. She presented a papular and scratched eruption on the trunk and upper extremities, associated with enlarged glands of the neck, axillae and groins. She had received many roentgen-ray treatments for the glands. The patient stated that one of the glands had been excised and showed Hodgkin's disease. The skin condition was improving under roentgen-ray treatment.

DISCUSSION

DR. HOWARD FOX said that the case might be considered one of Hodgkin's disease from the microscopic findings in the gland, though the clinical symptoms were not well marked. The eruption was of a prurigo-like type, frequently seen in both leukemia and Hodgkin's disease. They were the lesions that showed simple inflammatory changes, and not those characteristic of Hodgkin's disease. These cases of prurigo, as well as those of urticaria and pruritus, were probably toxic manifestations of the disease. When occurring in leukemia they had been termed leukemides by Audry.

DR. FRASER said that these prurigo-like eruptions were sometimes associated with Hodgkin's disease; but as Dr. Fox had stated, the histologic picture was neither that of leukemia nor of Hodgkin's disease, but an ordinary prurigo eruption. In other words, these lesions anatomically are not the Hodgkin's gland lesions. They are present as a complication.

DR. HIGHMAN said it was an unusually interesting case, for it brought to the fore in 1920 a condition established in Vienna in the eighties, described by Hebra and Kaposi as prurigo lymphatica, including the leukemias and Hodgkin's disease, or pseudoleukemia. The lesions were prominent on the flexor rather than on the extensor surfaces, which was characteristic, as opposed to the findings in typical prurigo. The case was not of the type that Audry

1. Arch. Dermat. & Syph. 1:151 (Feb.) 1920.

called the leukemides, but rather belonged to the true leukemic infiltrations. The former lesions were not characteristic of leukemia in their histologic structure; the latter were. He recalled two or three instances in which the histologic examination of the skin aroused suspicion of leukemia, later corroborated by the general findings. In this case there was a definite leukemic infiltration of the skin, and a clinical condition which European dermatologists would recognize without difficulty.

DR. WISE said that one of the interesting features of the case was that the patient gave a definite unmistakable history of having had enlarged glands which disappeared under roentgen-ray treatment, and subsequent to that therapy the skin disease appeared. One would not expect the lesions to come on after the disappearance of the glands. That impressed him as rather peculiar.

FOR DIAGNOSIS. From the service of Dr. Trimble, New York Skin and Cancer Hospital. Presented by DR. ROTHWELL.

The patient, a white man 56 years of age, presented over the dorsum of the trunk the dried crusts of pustules which had appeared two or three days after a slight fever and feeling of general malaise. He at the outset of his disturbance, noticed slight pain in the scapular (right) region, and at the outbreak of his pustular eruption he had experienced a slight chill.

The eruption, when first inspected, consisted of pustules generously distributed over the back, from the root of the neck to the waist, on distinctly erythematous bases. The limits of the eruption were posterior to the mid-axillary lines. A few pustular lesions were to be seen at this first inspection, distributed over the shoulders and on the outer aspects of the arms. The lesions had dried down under applications of simple boric acid ointment. There had been no other subjective symptoms than a feeling of contraction in the affected region.

DISCUSSION

Several of the members expressed agreement with the diagnosis of pustular folliculitis.

DR. ROTHWELL said he had not expected the case to attract so much interest. A number of physicians thought that it was simply a pustular folliculitis, but the diagnosis of double herpes zoster had been made by others.

DR. HIGHMAN thought the case looked like neither single nor double herpes zoster; clinically, it was suppurative folliculitis. In his opinion not much reliance could be placed on the patient's statement that no local applications had been used.

DR. WILLIAMS said there was a marked contradiction in the history. It was stated that the patient had had the eruption eight days only, and yet there were pale scars which could only result from lesions which had healed several weeks before.

A PRELIMINARY REPORT ON SILVER ARSPHENAMIN.* DR. MIRAN
B. PAROUNAGIAN.

Silver arsphenamin was first suggested by Ehrlich. The synthesis of this compound was completed by Kolle in 1918.

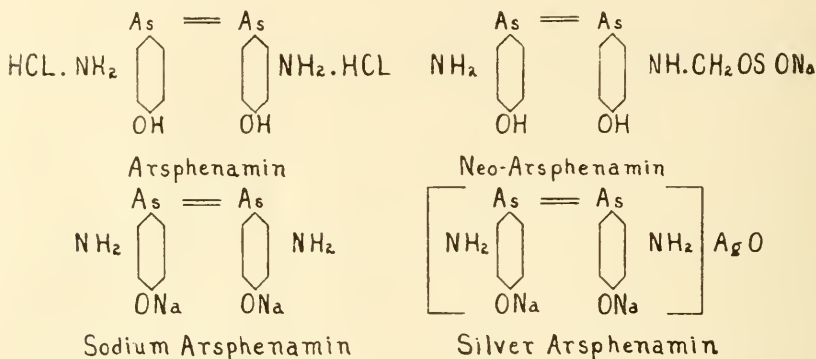
The drug was first tried by Wechselmann at the Speyerhaus, at Frankfort-am-Main. It has since been extensively used at many clinics in Germany.

* From the Department of Syphilology, Bellevue Hospital.

Reports of it are numerous in the German literature, and are practically unanimous in its praise. A résumé of the literature is reserved for a later communication.

The structural formula of silver arsphenamin is still under discussion by scientists abroad, particularly as regards the location of the silver in the molecule. There is no doubt, however, that the silver is actually chemically combined and not present in the product as finely divided or colloidal silver. The silver content is approximately 14 per cent. and the arsenic about 22 per cent.

For purposes of comparison the structural formulae of the various arsphenamin compounds are given:



In the formula for silver arsphenamin, it will be noticed that the entire molecule has been bracketed and the silver placed outside, indicating that its exact location has not yet been determined.

The dosage recommended by German investigators is from 0.1 gm. to 0.3 gm., and the intervals of treatment from twenty-four hours to four days. The number of injections is from eight to sixteen, according to the stage and resistance of the disease.

Through the courtesy of the H. A. Metz Laboratories, we have had the opportunity of administering silver arsphenamin made in America, according to the original formula.

Up to date, we have given 373 injections to 107 patients during a period of eight weeks. The dosage has varied from 0.05 gm. in children to 0.3 gm. in male adults. The dilution at first was 50 c.c. of 0.4 per cent. saline solution to each decigram. Later the dilution was decreased to 30 c.c. to each decigram. No difference in the action of the drug was noticed following this change in technic.

At first doses were given once weekly; later at five-day intervals, and more recently as often as every second day. The largest number of doses given to one patient has been eight, with a total dosage of 1.8 gm. The average patient has received to date about 1.5 gm., excluding those who have come under treatment within the past two weeks.

Patients with active lesions, who had received no previous treatment, were first selected in order to test clinically the therapeutic efficacy of this drug. Primary cases selected were positive for the *Spirochaeta pallida* by dark-field examination. The secondary cases were typical.

More recently patients with older and previously treated cases have been treated with this drug, although it has been our purpose to limit the use of silver arsphenamin to persons in whom the improvement could be determined clinically.

Early primary lesions of syphilis have responded with unusual rapidity to silver arsphenamin: within twenty-four hours the lesions have shown marked regression. In secondary cases ordinary roseolas have disappeared after one or two doses. Papular and pustular lesions have responded with gratifying rapidity. Mucous membrane lesions have been slightly more resistant. In late syphilis, ulcerating gummas, nodular syphiloderms and bone lesions have all responded satisfactorily to silver arsphenamin.

"Table reactions" have never occurred. Later ill effects have been uncommon, and in no case have they been serious. Mild headache, chill, nausea, vomiting and gastro-intestinal discomfort have occasionally been reported by patients, but these have always been of a mild type and in no instance was the course of treatment interrupted because of these by-effects.

In no case has mercurial treatment been combined with silver arsphenamin. Whether mercurial treatment will later be included in the routine is still under advisement. Reports from abroad are contradictory on this point.

The serologic result following the use of silver arsphenamin will not be considered in this preliminary report because, in our opinion, it is still too early to make any positive statement.

Summary.—1. Silver arsphenamin of American manufacture has been administered 373 times to 107 patients.

2. Uncomplicated primary lesions have shown marked improvement within from twenty-four to forty-eight hours.

3. Skin manifestations of the generalized period have been readily amenable to this drug.

4. Mucous membrane lesions of early syphilis have not disappeared with the same rapidity as the skin lesions of the same stage.

5. Later syphilitic manifestations improve satisfactorily under silver arsphenamin therapy.

6. None of the immediate table reactions nor the more serious later ill effects mentioned in the literature have been encountered in this series.

Conclusions.—In our hands silver arsphenamin has proved an effective addition to the arsphenamin series. Its small dosage, ease of administration, absence of ill effects and favorable therapeutic action will commend its further use, particularly by those adept in the use of other arsphenamin preparations.

Whether future experience will approve the use of silver arsphenamin alone or in combination with mercurial treatment remains to be determined.

DISCUSSION

DR. GOODMAN said that he had had the opportunity, through the courtesy of Dr. Phillip Grausman and Dr. Leo Michel, of using the German silver arsphenamin, and that he had with him several ampules of the drug which the members might care to examine. The drug had recently been brought over, and he had given it to seven patients. Two of them with primary lesions had shown improvement in a short time. A third patient with pustular secondary syphilis had improved in a manner which he had not seen exceeded by arsphenamin, except when that drug was given according to the method of Dr.

Pollitzer—three doses in forty-eight hours. Another patient with a +++ Wassermann reaction and possibly syphilitic disease of the sinuses had been given a dose on Sunday, and complained of a headache from Sunday to Monday morning. He regretted that roentgen-ray pictures of this patient prior to and after the injection were not available. No ill effect had been noted in connection with the injections of silver arsphenamin in the short experience he had had.

The German literature had mentioned many accidents following this drug. Allowing any of the solution to flow outside the vein and into the tissues was supposed to be attended with grave results. In several cases reported the drug had been given over long periods—sixteen to eighteen injections, and then by-effects were noted. On the whole, the reports had all been favorable.

DR. WISE said that what interested him was the question of argyria, and he would like to know what Dr. Parounagian had to say on that subject.

DR. BECHET wished to ask Dr. Parounagian if in his estimation the therapeutic results from silver arsphenamin were more satisfactory than those attained with arsphenamin; he had not mentioned this fact in his paper. Dr. Parounagian also spoke of the truly remarkable therapeutic results obtained in the short period of from twenty-four hours to two or three days; this was just as true for arsphenamin. Dr. Bechet recalled seeing a patient that same week with a large nodular serpiginous syphiloderm, several inches in diameter, to whom 0.9 gm. of neo-arsphenamin was administered. Within forty-eight hours the lesion had involuted more than 50 per cent. Dr. Parounagian had had some moderate reactions; these were becoming less and less frequent after the administration of arsphenamin. For the past two years not the slightest reaction had been observed by him; 0.9 gm. of neo-arsphenamin and 0.6 gm. of arsphenamin were the practically invariable doses.

DR. HIGHMAN said that the section should thank Dr. Parounagian for directing attention to the silver member of the arsphenamin group. He foresaw, however, danger in a new era of overenthusiasm followed by depression, such as had been gone through with arsphenamin. It reminded him of Perkins' metallic tractors which Oliver Wendell Holmes wrote about, and turtle bacilli—the only thing that would justify the introduction of a new preparation representing a material advance—something that could not be determined without statistics on which to base reasonable conclusions. The crux of the situation was: Was there less danger in the new than in the old salt; and did the lesions improve more rapidly, not just as rapidly? Why should a preparation that heals mucous lesions less rapidly than the old one be better, particularly since mucous membrane is more vascular than skin, which would justify the expectation of their more rapid involution than the skin lesions, as experience indicated with the old preparations. This seemed irreconcilable.

Dr. Highman said he could not gather any clear idea of Dr. Parounagian's time estimations; but that last Tuesday he had given a woman with a primary lesion on her hand and a florid secondary eruption, an injection of 4 dg. arsphenamin, and that by Friday the eruption had faded 80 per cent., and (if one could talk in such terms) the chancre had decreased by half in this same seventy-two-hour period. Were Dr. Parounagian's results any better than that?

DR. MACKEE said that silver arsphenamin was being used experimentally at the clinic, but they were not yet prepared to give out the results. Naturally he

was interested in this report by Dr. Parounagian, but was not much impressed with the results reported. It is curious how any new drug gives better results for a while, and later the results prove to be not so good. From what he had seen and read and heard, we have a drug that compares favorably with arsphenamin. About the danger, very little could yet be said. The question of argyria was an important one. We are getting keratoses from arsphenamin given a few years ago; and we may get argyria from using silver arsphenamin.

DR. ABRAWOWITZ said that in a conversation with Dr. Fordyce last spring regarding silver arsphenamin, the latter said that the possibility of argyria developing was to be considered. Lochte reports such a case of argyria, an abstract of which appeared in a recent issue of *The Journal of the American Medical Association*. The original case report was in the *Therapeutische Halbmonatshefte* **34**: (June 15) 1920.

DR. MACKEE said it was interesting to note the points of difference in observation. He had seen patients who had improved from 33⅓ per cent. to 150 per cent.; others say the patients do not improve at all. There is always a difference in the observations. Dr. Parounagian had just asserted that he had seen a chancre practically disappear within twenty-four hours. That seemed to be a biologic impossibility. He did not see how any lesion the size of a dime could undergo involution in twenty-four hours.

DR. HIGHMAN said he wished to corroborate the remark made by Dr. Lane. In 1915, when he was still working at Cornell University, a faculty rule had been passed forbidding larger doses of arsphenamin than 2 dg. Every one had been astonished to note that the results were precisely the same as with larger doses. Dr. Marsh had reported the findings, with these minimal doses in one of the New York medical periodicals. With such small doses were produced the same effect on all lesions as had been obtained from double the dose. Referring to Dr. MacKee's remarks about the disappearance of the chancre reported by Dr. Parounagian, Dr. Highman said that he also would like to know how a globule of infiltration the size of a small marble could be absorbed so soon, except under the eyes of enthusiasm.

DR. PAROUNAGIAN said, in reply to Drs. MacKee and Highman's remarks regarding the chancre healing in twenty-four hours that he was misunderstood, as he stated as follows: "Within twenty-four hours the lesions have shown marked regression." He conscientiously believed that the results from silver arsphenamin were far superior to either arsphenamin or neo-arsphenamin, either domestic or imported, and invited the gentlemen to visit his clinic and observe the cases.

As to Dr. Fred Wise's inquiry regarding argyria cases, he stated that he had seen an abstract of a case in *The Journal of the American Medical Association* from an article by Lochte, *Therapeutische Halbmonatshefte*. The patient had received seven neo-arsphenamin injections and ten months later developed tertiary lesions. Later he received twelve silver arsphenamin injections, the first injection intramuscularly; five days later icterus developed and in spite of that the injections were continued; a few days later argyria developed. Dr. Parounagian said, taking into consideration thousands of injections that have been given in Germany, the one or two cases of argyria reported was not as serious as the number of deaths reported from the use of arsphenamin and neo-arsphenamin.

PHILADELPHIA DERMATOLOGICAL SOCIETY

*Regular Monthly Meeting, Jan. 10, 1921*MILTON B. HARTZELL, M.D., *Presiding*

LICHEN PLANUS. Presented by DR. HARTZELL.

A white girl, 10 years of age, developed an eruption last July, which rapidly became generalized, though the face, hands and feet have remained relatively free. Until a few days before presentation, when she came under the speaker's observation, she had received no internal medication, using only a liniment prescribed by the attending physician. At first the rash was very itchy, but later that symptom abated somewhat. The outbreak consisted of almost innumerable pinhead sized shiny papules and pigmented areas from which similar lesions had disappeared. The present papules and stains of former ones were definitely grouped into areas 0.5 to 1 cm. in diameter, the groups being equidistant from one another, about a centimeter apart on the back, where they were most abundant. In some places distinct rings were seen but there was no linear arrangement or umbilication. There was a slight degree of elevation of the lesions, which was most apparent on the trunk, especially posteriorly. The outbreak on the extremities was much fainter and less thickly-set. Scaling was slight or absent. The speaker had never seen a similar case. He considered it an atypical lichen or lichenoid eruption.

DISCUSSION

DR. SCHAMBERG said he had never seen a similar case, at least in a child. Many of the papules had a perifollicular position.

DR. ROSE HIRSCHLER asked Dr. Hartzell the age of the youngest patient with lichen that he had seen. He replied that he could not answer definitely, but that he had never seen it in infancy. In this case there was a fine stippling due to atrophy about the mouths of the follicles. There was no mucous membrane involvement. The case was unique in his experience.

STRIAE ATROPHICAE. Presented by DR. STRAUSS.

The patient was a well built man of 24 without an excessive deposit of adipose tissue. He had not varied more than 3 or 4 pounds in weight since the eruption was noticed, and he had at no time taken on weight rapidly. In March, 1920, he first noticed the eruption which had appeared on the inner aspects of both thighs. When seen at that time it consisted of slightly depressed purplish and reddish streaks, running somewhat transversely and corresponding roughly to the lines of cleavage of the skin. Since that time they had paled considerably, and bore more resemblance to depressed, stretched scars. There were no subjective symptoms, and there was no similar eruption on the lower abdomen or other portion of the body. The case was shown, not so much for diagnosis as for explanation of its appearance in this region apparently without cause. Those present offered no opinion.

ATROPHODERMA PEMPHIGOIDES. Presented by DR. GREENBAUM for DR. SCHAMBERG.

The Jewish woman, aged 55, shown at the November and December meetings of the society, was the patient. After three months' observation the

attendants had finally been able to overcome her prejudices sufficiently to allow them to aspirate one of the lesions on her leg. Some bloody serum escaped. Until that time, there had been some doubt among the members as to whether the lesions were really blebs. Only a few drops of contents escaped as the bleb was somewhat flaccid.

DISCUSSION

DR. HARTZELL still hesitated to classify the eruption or the lesion as a bleb on account of its peculiar characteristics.

DR. SCHAMBERG agreed that it was not an ordinary bleb, but felt that the name *atrophoderma pemphigoides* was applicable to the condition; a bleb followed by atrophy, the latter deep and the lesions remarkable. Dr. Hartzell added that it did not appear to be an inflammatory lesion.

DR. HIRSCHLER had not seen the case before. She remarked on the sensation of an edge produced when the finger was passed over the lesions—a buttonhole left by the deep atrophy.

DR. GREENBAUM added that the condition was now in its third year. Occasionally, new blebs had made their appearance while the patient had been under observation, and these ran an indolent course. Even the smallest ones had the same quality as the large ones—deep atrophy in the corium. Individual lesions had lasted at least three months.

DR. SCHAMBERG remarked that to some it might suggest an adult case of *epidermolysis bullosa*, but in the latter disease there would be a history of injury and the blebs would be superficial.

DR. HARTZELL ended the discussion by saying that it was all guesswork without a biopsy, consent for which procedure would be almost impossible to obtain from this patient, judging by the length of time necessary to effect aspiration of a bleb.

ATROPHIA CUTIS. Presented by DR. CORSON.

A waiter, Russian by birth, who had been seen that day for the first time, had had several attacks of gonorrhea—one or more during the course of the skin condition. This outbreak was limited to the glans penis and the sulcus behind it. The patient said it started as reddish, scaly areas on the glans and gradually covered its surface. Later the color faded, the scale disappeared and when shown the skin of the glans was thinned, loose, cracked and somewhat shiny. In addition, there were a number of small depressed scars on the surface. The patient was circumcised in infancy, and insisted that he had kept the glans clean when he had a urethral discharge. No caustics had even been used on the penis.

DISCUSSION

DR. SCHAMBERG said the condition resembled scarring due to superficial erosive action.

DR. HIRSCHLER said she had noticed such superficial scarring of the genitalia in women—both gonorrhea and chancroidal cases.

CASE FOR DIAGNOSIS. Presented by DR. KLAUDER.

A mulatto woman, aged 25 years, presented a maculopapular rash, generalized in distribution and of three months' duration. She had originally undergone treatment as a syphilitic patient and had received thirty injections of

arsphenamin when the present outbreak appeared. Since that time, seven more injections had been given. The lesions scattered over the body were not numerous, probably not exceeding twenty-five. They ranged in size from that of a pea to that of a large lima bean. In color, they were dark reddish-brown with a well-defined scale. Itching was complained of, and the lesions were lightly excoriated. They were somewhat elevated and plaque-like. The trunk and arms were the seat of most of the lesions.

DISCUSSION

DR. SCHAMBERG brought up a point of interest as to whether there was any relation between the arsenical treatment and the eczematoid dermatitis en plaque which this condition resembled. If caused by the drug, the lesions would, following its withdrawal, tend to disappear and later recur at the same place on resumption of treatment, acting as a danger signal preceding a generalized outbreak. Here the eruption resembled more the eczematoid type in that it was unaffected by arsphenamin treatment.

DR. KLAUDER said a cutaneous test for arsphenamin sensitization had been employed with negative results.

DR. HARTZELL thought it unusual that an acute arsenic dermatitis should occur in circumscribed patches. The lower part of the legs was free from eruption. General adenopathy was still present.

DR. SCHAMBERG said that organic arsenic preparations sometimes affected small areas of skin, citing the instance that the backs of the fingers sometimes show patches of dermatitis, no other region being affected.

DR. C. N. DAVIS remarked that the case resembled the so-called parasitic eczema of some European observers.

DR. KLAUDER explained that this patient had received no mercury. Following extravasation, there was a patch of pigmentation with some thickening at the bend of the elbow. At the December meeting, Dr. Schamberg had pointed out the possibility of cases of arsphenamin dermatitis having been sensitized in this manner. This patient was unaffected by subsequent treatment—neither better nor worse. The dosage was 0.6 gm. arsphenamin throughout.

ACNE NECROTICA. Presented by DR. GREENBAUM.

A short, stout, Jewish girl of 12 years had an eruption of one year's duration, situated on the upper part of the back and on the forehead at the hair margin, scattered from ear to ear. The back showed nothing but the depressed scars where active lesions had recently existed. These cicatrices averaged the size of a split pea. On the forehead flat, crusted lesions were interspersed with other depressed scars of a slightly smaller size. When first taken under observation, the pustules on the back were active and were seen to heal and change into the present formations.

DISCUSSION

DR. HARTZELL said he had never seen such large cicatrices resulting from this disease. The scars were clearly due to this eruption as some active and infiltrated lesions could still be seen. They were papules with a necrotic center which left a central pit. There was none on the hands where papulonecrotic tuberculid was frequently found.

DR. GREENBAUM found the *Staphylococcus aureus* in cultures from the lesions.

DR. SCHAMBERG remarked that this appearance was frequently seen in Russian emigrants in some of which he had suspected an infected varicella at

some previous time. The small follicular pits in the larger depressions made them look not unlike vaccination scars. They were not in the group with papulonecrotic tuberculids, and he did not regard them as tuberculous in origin.

DR. HARTZELL felt that there was apparently some relation between the two conditions, but so far he had not been able to trace it. The lesions were not like the papulonecrotic tuberculid on the hand.

DR. SCHAMBERG observed that acne necrotica is cured in a relatively short time. It responds readily to roentgen rays and vaccines. This is not the case with the papulonecrotic tuberculid which is more resistant. Among other diseases of the skin caused by the tubercle bacillus or its toxin, he felt that lupus erythematosus should be included. He was more and more persuaded to believe that this was the case. It was hard to remove this factor in the face of the knowledge that 90 per cent. of mankind have or have had the disease. Whether it was the first or second factor in the causation, he did not know.

DR. HARTZELL said that he had had cases of lupus erythematosus in persons with excellent physique, the disease lasting thirty years in one instance. He did not believe it was due to tuberculous infection. Against the fact of almost universal infection can be advanced the argument that in that case, the disease should be much more common. Many cases were undoubtedly aggravated or known to occur after sunburn.

DR. SCHAMBERG reported that the negro with the prurigo-like eruption, enlarged lymph nodes and lipomatosis, shown at the November meeting had an eosinophilia of 58 per cent. which later fell to normal and subsequently rose to 43 per cent. The eruption was accentuated at the time of the paroxysm of eosinophilia.

Book Review

VENEREAL DISEASES, THEIR CLINICAL ASPECT AND TREATMENT. With an Atlas of 108 colored and 21 halftone illustrations. By J. E. R. McDONAGH, F.R.C.S. St. Louis, C. V. Mosby Company, 1920.

McDonagh has given us a companion volume to his earlier book, "The Biology and Treatment of the Venereal Diseases," which was published in 1915. Like the first volume, it is an expression of personal opinion. He starts in directly with the "leucocytozoon syphilidis" etiology of syphilis without any preliminary statement for the many persons who may be unacquainted with McDonagh's generally unaccepted theory of the sexual and asexual cycles of this supposed organism.

The clinical material on which the book is based appears to be uncommonly great in amount and comprehensive in character. Every phase of syphilis is considered. The drugs used in the treatment of syphilis include, besides mercury and arsphenamin, the various preparations which McDonagh has exploited. His therapeutics are as queer as his microbiology of syphilis and as little in accord with accepted views. The book cannot be recommended to the uninitiated in the knowledge of syphilis. It is more or less stimulating to the expert from the very fact of its radical views. If McDonagh is in step the rest of the regiment is certainly out of step.

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A STUDY OF THE HISTOLOGIC CHANGES PRODUCED EXPERIMENTALLY IN RABBITS BY ARSPHENAMIN *

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The fatalities among persons following the administration of arsphenamin and neo-arsphenamin in the treatment of syphilis, have been mainly attributed to the toxicity of the drugs and to technical errors in administration referable to the preparation of the solution and manner of injection. The results of studies of the gross and histologic tissue changes have usually shown the presence of some form of acute nephritis and degenerative changes in the liver as the most prominent lesions. In Europe an acute hemorrhagic and "serous" meningitis or, rather, an acute meningeal congestion, has been commonly described, whereas in America few or no changes in the membranes and substances of the brain and cord have been found. Under these circumstances, however, only limited information can be gained regarding the tissue changes ascribable to the solutions of the drugs because of pathologic changes in the organs and tissues due to syphilis, for which the majority of persons succumbing after injections of arsphenamin have been treated.

VALUE OF EXPERIMENTAL STUDIES

A study of the effects of arsphenamin and neo-arsphenamin on the tissues of experimental animals has proved of interest in two main

* From the Dermatological Research Laboratories of Philadelphia and the McManes Laboratory of Pathology of the University of Pennsylvania.

* Investigation aided by funds accruing from the preparation of arsphenamin.

directions, namely, as bearing on the methods of treatment of syphilis with these compounds and on the subject of specific arsenic therapy.

For example, in reference to the treatment of syphilis, differences in the degree of tissue changes, which were sometimes quite evident, have been found after the intravenous injection of arsphenamin and neo-arsphenamin, and profound differences have been observed according to the kind of solution of arsphenamin administered, as acid and alkaline (disodium) solutions.

In reference to the subject of chemotherapy, we agree with Wade Brown¹ who has well said that the determination of toxicity of new compounds for experimental animals in so far as duration of life is concerned, is insufficient, and that the question of tissue injury has not attracted the attention that the subject deserves.

In comparative study of the changes occurring in the kidneys and suprarenals of experimental animals by various arsenical compounds, Pearce and Brown,² have shown that there may be but slight relation between toxicity and tissue injury and that one may be diminished without necessarily reducing the other; according to their results, it is doubtful whether there is as yet a single compound of arsenic possessing curative value in experimental trypanosomiasis that produces neither toxic symptoms nor organic tissue changes.

The purpose of the experimental chemotherapeutist is, therefore, the production of compounds possessing the maximum of curative value for a certain infection with the minimum of toxicity and tissue injury for experimental animals and persons.

PURPOSES OF INVESTIGATION

The present investigation is a continuation of a series of studies by one of us (Kolmer) with Schamberg and Raiziss,³ bearing on the

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comparative toxicity and curative activity of arspnenamin and neo-arsphenamin from the standpoint of treatment of disease and in relation to experimental chemotherapy with new arsenical compounds being prepared and studied in these laboratories.

In this article are given the results of studies bearing on the histologic changes produced in the tissues of rats and rabbits by different solutions of arspnenamin administered in single large and multiple small doses; the results of a similar study with neo-arsphenamin are given separately.⁴

EXPERIMENTAL

White rats and rabbits were employed in all experiments. Arspnenamin was administered by injection into the saphenous veins of rats with a gravity apparatus, in the form of 2 per cent. solutions in freshly distilled water at the rate of 0.5 c.c. per minute; rabbits were injected with a syringe by way of the ear veins. Both acid (non-neutralized) and alkaline (disodium) solutions were administered. In preparing the latter the technic of the Hygienic Laboratory was employed, namely, the addition of 0.9 c.c. of a solution of normal sodium hydroxid for each 0.1 gm. of drug; this amount of alkali represents an excess of that required for neutralization and results in a solution of the disodium compound of arspnenamin.

Some of the animals were killed at varying intervals after injection and usually by a very brief exposure to illuminating gas which appeared in comparative tests least likely to induce tissue changes, as a number of control animals killed in this manner never exhibited any discernible gross or minute tissue changes. Some animals succumbed at varying intervals after injection; necropsy examinations were performed on these within a few hours after death, and the tissue changes were always identical with those encountered in animals destroyed at chosen intervals by a brief (stupefying) exposure to illuminating gas.

Necropsy examinations were performed immediately after death, and the following organs divided into two parts and placed in Orth's fluid, and in 5 per cent. neutral liquor formaldehydi: cerebrum, cerebellum, brain stem and meninges, lungs, heart, liver, spleen, suprarenals and kidneys. Paraffin and frozen sections were prepared, sections being made of each organ at varying levels; considerable preliminary study was required for the determination of the best technic for the various tissues from the two species of animals. Special studies were made of the suprarenals in reference to the chromaffin

4. Kolmer, J. A., and Lucke, B.: A Study of the Histologic Changes Produced Experimentally in Rabbits by Neo-Arspnenamin, *Arch. Dermat. & Syph.*, this issue, p. 515.

cells and also of the lipid contents, frozen sections being stained with Herzheimer's scharlach r for the latter. Paraffin sections were routinely stained with hematoxylin and eosin.

The tissues of several series of normal rats and rabbits of the same weights and ages as employed in our experiments were studied preliminary to the experimental part in order to have the histologic variations of the different organs under normal conditions for comparative study.

Considerable variation in the degree of tissue change was found among animals of the same species receiving the same drug in the same manner and at the same time; for this reason detailed descriptions may be advisable, but would greatly extend the present article so that a résumé or summary of the changes in the different organs viewed as a whole is here presented.

RESULTS

HISTOLOGIC CHANGES PRODUCED BY THE INTRAVENOUS INJECTION OF ACID SOLUTIONS OF ARSPHENAMIN

When arsphenamin is dissolved in water the solution is acid and very toxic for all experimental animals; in previous studies, Schamberg, Kolmer and Raiziss⁵ have determined that failure to neutralize solutions of arsphenamin with alkali leads to an increase in toxicity of from 50 to 60 per cent. in solutions of 0.5 to 1 per cent. concentration. A few of the fatalities among human beings have been ascribed to the intravenous injection of acid solutions; in our experiments relatively large doses were employed and all of the animals, excepting one, died within a few minutes after the completion of the injections.

TABLE 1.—THE INTRAVENOUS INJECTION OF ACID SOLUTION OF ARSPHENAMIN IN RATS

Weight, Gm.	Sex	Dose per Kilo	2 Per Cent. Solution, C.c.	Results
105	F	0.100	0.53	Immediate death
140	M	0.090	0.63	Immediate death
85	M	0.080	0.34	Killed 12 hours later
95	M	0.070	0.33	Immediate death
130	M	0.060	0.39	Immediate death
110	M	0.050	0.28	Immediate death

Table 1 gives the results observed after the intravenous injection of acid solutions of arsphenamin in rats and Table 2, of similar injections in rabbits; the tables show the doses employed.

5. Schamberg, J. F.; Kolmer, J. A., and Raiziss, G. W.: Experimental and Clinical Studies of the Toxicity of Dioxydiamino-Arsenobenzol Dichlorhydrate, *J. Cutan. Dis.* **35**:286 (May-June) 1917.

TABLE 2.—THE INTRAVENOUS INJECTION OF ACID SOLUTION OF ARSPHENAMIN IN RABBITS

Weight, Gm.	Dose per Kilo	2 Per Cent. Solution, C.c.	Results
1,580	0.030	2.4	Died at once
2,660	0.040	5.3	Died at once
1,650	0.050	4.1	Died at once
2,450	0.060	7.4	Died at once
1,740	0.080	7.0	Died at once

The principal tissue changes were:

Cerebrum, Cerebellum, Brain Stem and Meninges.—In both rats and rabbits hyperemia of the meninges, and especially of the pia-arachnoid, was found; in many of these vessels were conglutinated or even hyalinized masses of erythrocytes in which the outlines of the individual cells were poorly defined or entirely lost. Occasional small hemorrhagic areas were found in different parts of the brain and in the meninges. Thrombi of conglutinated erythrocytes were also found in some of the smaller vessels of the cerebrum and cerebellum, but there were no discernible changes in the ganglion cells.

Lungs.—Vascular changes were most prominent. The majority of the blood vessels contained thrombotic masses, often possessing a light yellowish green color and in the larger vessels presenting a peculiar whorl-like appearance (Figs. 1, 2, 3, 4). The bands of these thrombi were usually homogeneous, but were sometimes granular; individual erythrocytes were only occasionally to be discerned. The capillaries of the alveolar walls in some areas were engorged with conglutinated erythrocytes; in other areas they were quite empty and even collapsed. Hemorrhage into the air sacs and interstitial tissue was found in only a few scattered areas; no other changes of importance were present.

Heart.—The most prominent changes were distention of the right auricle and ventricle with clots composed of more or less conglutinated erythrocytes; embedded in these clots were found the same peculiar yellow-green tinted whorl-like bands of homogeneous material seen in the larger pulmonary vessels (Fig. 5). These "acid-arsphenamin thrombi" were different in morphology and staining from the ordinary "hyalin thrombi" frequently found in various toxic and infectious diseases. The capillaries of the heart wall were generally intensely congested, and many contained conglutinated or hyalinized masses of erythrocytes. In a few instances rupture of capillaries with resulting small focal hemorrhages between the muscle bundles were encountered. Here and there anemic areas were found, apparently due to vascular occlusions.

Liver.—Intense hyperemia and widespread but irregularly distributed vascular occlusion, with conglutinated and partly or entirely hyalinized masses of erythrocytes, characterized the most conspicuous alterations (Fig. 6). In view of the tissue changes found in many animals of the other experimental series, this irregular thrombosis is to be emphasized. Most often the central lobular veins and the capillaries around these vessels were prominently distended, either with fairly well preserved erythrocytes, or, more frequently, with red cells more



Fig. 1.—Lung from rabbit injected with acid arsphenamin; immediate death. All the larger vessels are occluded by thrombi, details of which are shown in Figures 2, 3 and 4. (Very low magnification.)

or less fused or even hyalinized. Sometimes the peripheral vessels (the branches of the hepatic artery and portal vein and the peripheral capillaries) were similarly distended, while the central lobular veins and the adjacent capillaries were almost empty. No changes in the liver cells were discernible when death followed immediately after the injection, but in the one animal which survived five hours, early necrotic changes were observed in numerous irregularly distributed areas but

particularly around the intralobular veins. These areas gave the impression of early infarctions and were sometimes flooded with escaped erythrocytes.

Kidneys.—Marked congestion and large numbers of thrombi of conglutinated erythrocytes mainly in the vessels of the boundary zone, constituted the predominating change; the malpighian tufts were usually greatly engorged and generally filled the capsular space. Many of the component capillaries contained hyalinized or conglutinated erythrocytes, while others were without contents and collapsed. Hemorrhages were

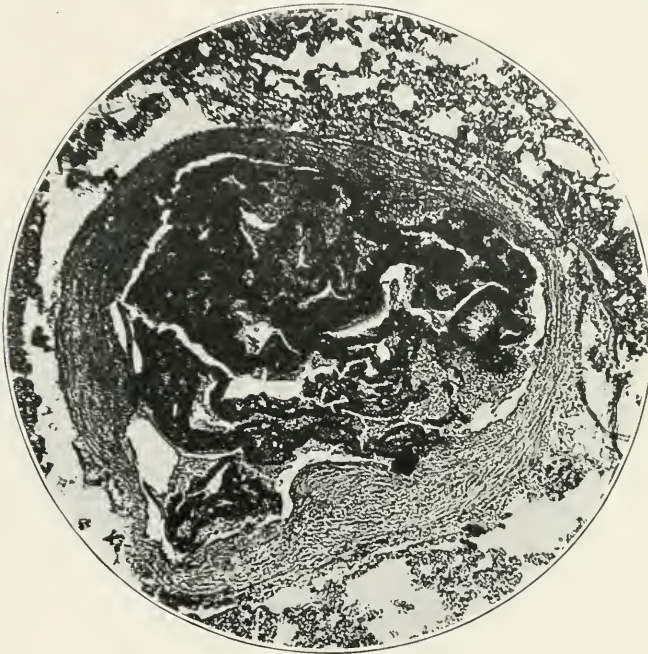


Fig. 2.—Large pulmonary artery from rabbit injected with acid arsphenamin; immediate death. Occlusion with a peculiar type of thrombus which consists of light yellow-green colored homogeneous bands arranged in a whorl-like formation ("acid-arsphenamin thrombus"). (High dry lens magnification.)

not found; changes in the tubular epithelium were not observed except in the one animal that survived five hours, marked cloudy swelling and coarse granularity of the cells of the convoluted tubules especially being encountered.

Suprarenals.—The only prominent and constant change was well marked congestion of the medullary portion, with numerous small thrombi similar to those found in the other organs; there were no discernible changes in the lipoid and chromaffin contents.

Spleen.—This organ usually showed an intense congestion and numerous thrombi of conglutinated erythrocytes; the follicles and trabecula presented no changes.

HISTOLOGIC CHANGES PRODUCED BY THE INTRAVENOUS
INJECTION OF SINGLE LARGE DOSES OF SOLU-
TIONS OF DISODIUM ARSPHENAMIN

In the routine toxicity tests of arsphenamin white rats weighing from 100 to 150 gm. are injected with 2 per cent. solutions of disodium arsphenamin in doses equivalent to 0.1000 gm. per kilogram of body



Fig. 3.—Large pulmonary artery and part of veins from rabbit injected with acid arsphenamin; immediate death. Both vessels are occluded with thrombi of the type shown in Figure 2. (High dry lens magnification.)

weight; this amount is equivalent to 6 gm. per 60 kilos of body weight. The tissues of rats succumbing at varying intervals after these injections, as shown in Table 3, have been examined as part of our study.

As a general rule, rabbits are somewhat more susceptible to the toxicity of arsphenamin. A number were given intravenous injections of 0.080 gm. of disodium arsphenamin per kilo of body weight, corresponding to 4.8 gm. per 60 kilos, and examined at varying intervals after injection, as shown in Table 4.

In some instances the animals had been dead about twelve hours before necropsy examinations were performed; however, the majority of animals were killed at intervals and the necropsy examinations were performed within an hour.

TABLE 3.—THE INTRAVENOUS INJECTION OF RATS WITH SINGLE LARGE DOSES OF SOLUTION OF DISODIUM ARSPHENAMIN

Weight, Gm.	Sex	Dose per Kilo	Results
100	M	0.100	Lived 2 days
125	M	0.100	Lived 10 days
100	M	0.100	Lived 11 days
110	M	0.100	Lived 12 days
150	M	0.100	Lived 13 days

TABLE 4.—THE INTRAVENOUS INJECTION OF RABBITS WITH SINGLE LARGE DOSES OF SOLUTIONS OF DISODIUM ARSPHENAMIN

Weight, Gm.	Dose per Kilo in 10 C.c.	Results
1,690	0.080	Examined 3 days after injection
2,230	0.080	Examined 5 days after injection
1,640	0.080	Examined 7 days after injection
2,150	0.080	Examined 12 days after injection

The histologic changes may be summarized as follows; marked differences were found according to the duration of life following the injections:

Cerebrum, Cerebellum, Brain Stem and Meninges.—Sections of different portions of the cerebrum and cerebellum have shown no striking or constant changes. The brain vessels were moderately engorged in some animals; here and there clear zones of perivascular edema were found. Occasionally a few isolated degenerated ganglion cells were encountered. The meninges have generally shown well marked congestion and a few hyalinized thrombi. Slight meningeal edema and occasional small round cells were often encountered, but leukocytic infiltration was not seen in any section. In two animals surviving for more than ten days several minute hemorrhages were found in the brain substance.

Lungs.—Vascular changes were most prominent but varied according to the duration of life after the injection of arspnenamin; these changes were also somewhat more marked among the rats than among the rabbits.

When the lungs were examined within two days after injection of arspnenamin, marked congestion and small thrombi of conglutinated erythrocytes were seen associated with scattered areas of edema and extravasation of erythrocytes into the air sacs. After longer intervals

between injection and death less marked congestion and edema were usually found. Catarrhal swelling and inconspicuous desquamation of the lining alveolar epithelium was frequently encountered. Thrombosis was practically never seen. The terminal bronchi and bronchioles frequently exhibited slight mucopurulent inflammatory changes; the latter, however, may not have been caused by the drug.

Heart.—No constant and striking changes were found; the epicardium and endocardium appeared normal, but in a few animals, and especially among the rats that died within a few days after injection,

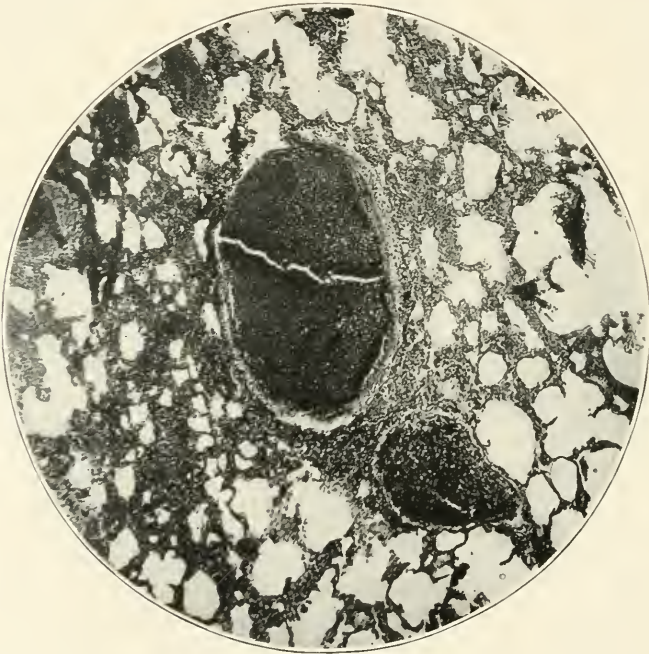


Fig. 4.—Large pulmonary artery and veins from rabbit injected with acid arsphenamin; immediate death. The erythrocytes are partly conglomerated and in places fused into hyaline masses. Thrombi of this type occur frequently with the peculiar "acid arsphenamin thrombi" shown in Figures 2 and 3. In Figure 1 "conglutination," "hyaline" and "acid arsphenamin thrombi" are shown. (Low dry lens magnification.)

small areas of focal parenchymatous degeneration were encountered in the myocardium. In these areas the muscle cells appeared cloudy, swollen, hyalinized, vacuolated, devoid of striations, and presented nuclear degeneration. In some instances the smaller vessels were congested and occasionally plugged with thrombi of conglomerated erythrocytes, which were probably responsible for the areas of focal degeneration. In several animals rather diffuse cloudy swelling of the



Fig. 5.—Clot in right ventricle from rabbit injected with acid solution of arsphenamin; immediate death. Embedded in the mass of partly conglutinated erythrocytes are the yellow-green colored, homogeneous bands of the "acid arsphenamin thrombi." (Low dry lens magnification.)



Fig. 6.—Liver from rat injected with acid arsphenamin; immediate death. Extreme congestion and occlusion of the central lobular veins and intralobular sinusoids with conglutinated and partly hyalinized erythrocytes. The blood channels of the organ stand out as boldly as if they were injected with a coloring mass. (Low dry lens magnification.)

muscle fibers were seen; slight swelling of the vascular endothelium sometimes occurred. In one rat, succumbing after ten days, an area of necrosis with well marked infiltration by small round cells and fewer polymorphonuclear leukocytes was present.

Liver.—The liver has shown extensive and striking changes in all animals, but particularly among the rats; these changes were mainly in the form of extensive areas of coagulation necrosis involving all parts of the lobule but particularly the central and middle portions.



Fig. 7.—Liver from rat injected with a single large dose of disodium arsenophenamin; death two days after injection. There is a massive necrosis involving all but the lobular peripheries. (Low dry lens magnification.)

Rats succumbing within two days after the injection have shown changes so extensive as to resemble those commonly found in acute yellow atrophy, entire lobules, excepting the most peripheral portions, being necrotic and sometimes flooded with erythrocytes and infiltrated with mononuclear and fewer polynuclear leukocytes (Fig. 7). Among animals surviving a week or longer, the areas of necrosis were not so

large but were found in various parts of the lobule including the peripheral portions (Figs. 8 and 9). The irregular distribution of these necrotic areas is noteworthy.

The different stages of the necrotic process could be well recognized. The earliest changes occurring in animals that survived only a day or two were extensive coagulation necrosis, probably due to infarction. Later complete breaking down of the necrotic portions occurred, which then became flooded with erythrocytes and invaded by various phago-

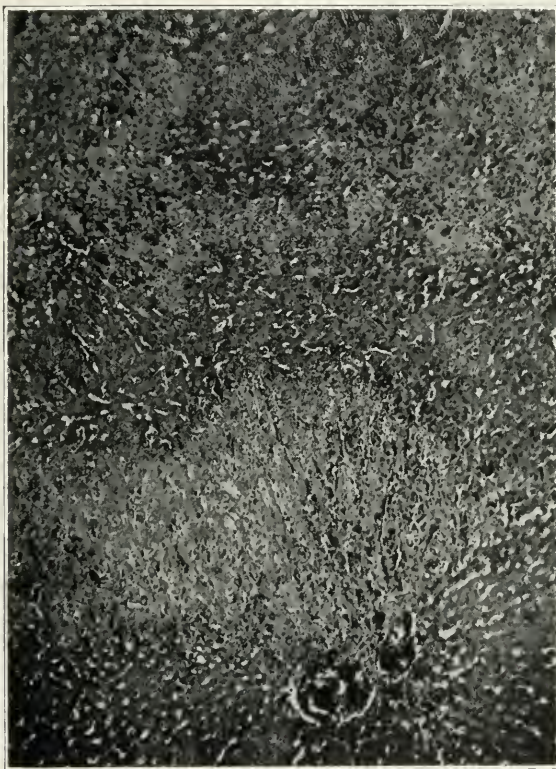


Fig. 8.—Liver from rat injected with a single large dose of disodium arspenamin; death ten days after injection. Many large irregularly distributed areas of necrosis are present, some are partly flooded with erythrocytes. (Low dry lens magnification.)

cytic cells. The bile ducts usually showed no changes other than occasionally swollen epithelium. Many of the animals presented portal, as well as intralobular, congestion. Thrombi of conglutinated and hyalinized corpuscles were frequently seen in the vessels of the capsule, within the lobules and in the necrotic areas. Inconspicuous perilobular fibrosis was encountered only among animals surviving ten days or longer.

Kidneys.—Marked degenerative changes were generally found in all animals, but the kind and severity of the changes varied according to the duration of life following the injection of arsphenamin; as a general rule, the kidneys of rats showed somewhat greater changes than those of rabbits, although this may be expected by reason of the larger doses administered to the former.

Among animals succumbing within two days after injection, vascular changes predominated; among those living for longer intervals,

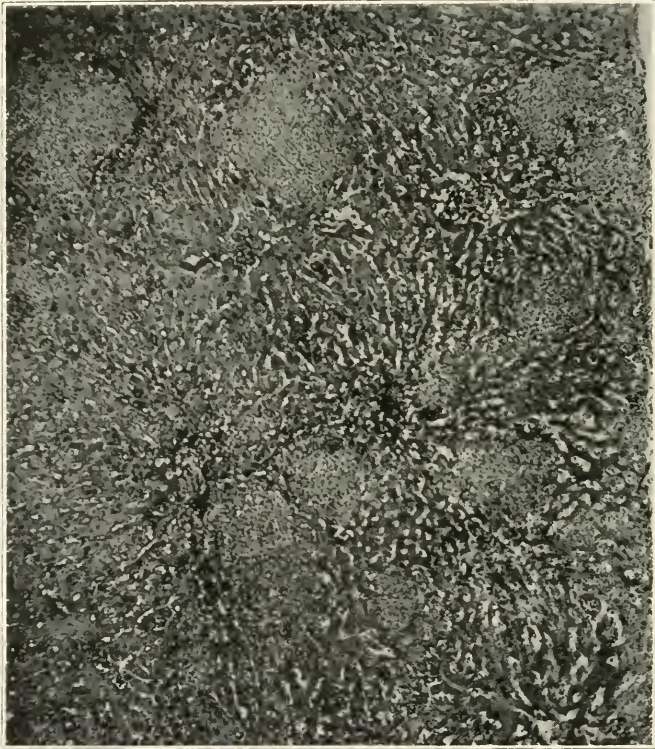


Fig. 9.—Liver from rat injected with a single large dose of disodium arsphenamin; death eleven days after injection. Many areas of irregularly distributed necrosis are present. (Low dry lens magnification.)

tubular degeneration was more prominent with marked variations in the severity and extent of the lesions.

The vascular changes consisted principally of marked congestion of the vessels of the boundary zone and cortex; occasionally minute interstitial hemorrhages were seen. Numerous small thrombi of conglutinated erythrocytes were encountered. The glomerular tufts were generally greatly engorged and in part occluded with hyalinized

thrombi; some of the loops were collapsed. The capsules of Bowman usually showed no changes of the lining epithelium, but some fluid and granular débris were frequently found in the intracapsular space. Even in the animals dying after a short period, pronounced degeneration of tubular epithelium occurred, but the parenchymatous changes were generally greatest in animals surviving for a week or longer. The mildest changes consisted of extensive cloudy swelling, vacuolization and granularity, involving particularly the convoluted tubules of the inner cortical zone. While the limbs and loops of Henle sometimes showed considerable cellular degeneration, this change was never as pronounced as in the convoluted tubules. The collecting tubules were least affected.



Fig. 10.—Kidney from rabbit injected with a single large dose of disodium arspenamin; death ten days after injection. Large patches of the cortex are entirely necrotic and heavily infiltrated with calcium salts (which take a black tint in the photograph). The medullary portions of the kidneys were never necrotic. (Very low power magnification.)

The degenerative alterations were of all degrees; several animals surviving about five to seven days showing almost complete necrosis of the outer half of the cortex. The necrotic regions were heavily infiltrated with lime salts (Figs. 10, 11 and 12).

A curiously irregular distribution of the tubular degeneration and necrosis was noted. Thus, often only isolated tubules were necrotic

while the neighboring tissue was in a fair state of preservation. In many instances the distribution was such as to point to infarction (Figs. 13 and 14).

In the extreme necrosis all elements of the renal tissue in the involved areas were completely destroyed.

Granular debris, erythrocytes, and desquamated cells frequently formed tubular casts.



Fig. 11.—Kidney from a rabbit injected with a single large dose of disodium arsphenamin; death eleven days after injection. Great necrosis of cortical regions, which are heavily infiltrated with calcium salts (black in the photograph). In an attempt to bring out the necrotic portions some of the intervening tissue is thrown out of the proper focus. (Low dry lens magnification.)

Slight edema was often found. The various changes pointed strongly to individual difference in susceptibility or resistance among the animals.

Among the kidneys of animals surviving about two weeks, slight interstitial fibrosis was evident in both cortex and medulla, and especially about areas of marked tubular necrosis.

Suprarenals.—In practically all animals there was great alteration in the lipoid and chromaffin contents.

Among the animals surviving about two days the lipid material was present only in the inner border of the zona fasciculata and occurred chiefly in the form of large droplets. In the zona glomerulosa the cells were almost entirely free of lipid substances. Among the animals surviving for ten days or longer the lipid material was likewise changed from finer granules to coarser droplets and showed evidences of depletion, being principally limited to the outer or inner border of the zona fasciculata.

The chromaffin contents of the medullary cells was diminished, more especially in the animals surviving for five days or longer, indi-

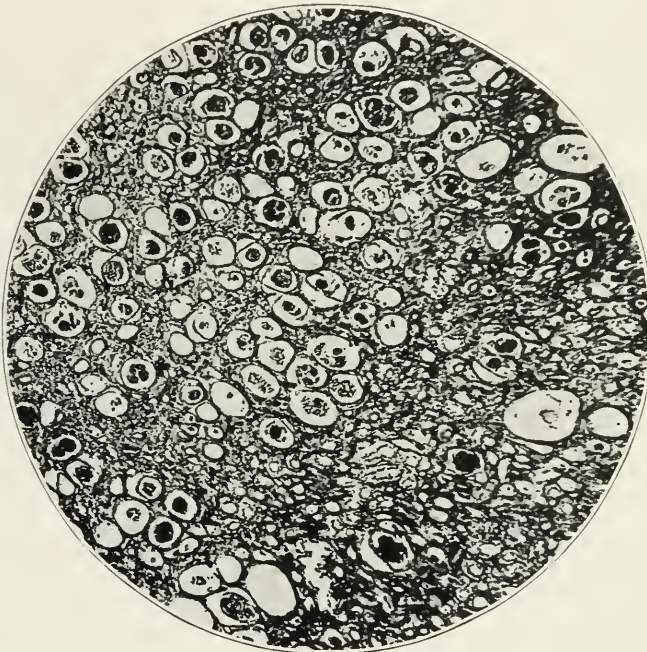


Fig. 12.—Kidney from rabbit injected with a single large dose of disodium arspenamin; death eleven days after injection. A portion of the renal medulla is shown; many collecting tubules contain casts composed chiefly of conglutinated erythrocytes and necrotic renal epithelium. (Low dry lens magnification.)

cating a gradual rather than sudden exhaustion, although this change was not constant.

Many of the cells in both medulla and cortex showed cloudy swelling and nuclear degeneration.

Many of the suprarenals showed moderate congestion of the medulla and cortex, particularly of the former, and a few small thrombi of conglutinated erythrocytes.

Interstitial changes, such as cellular infiltrations and fibrosis, were not encountered.

Spleen.—These organs frequently presented striking irregular areas of coagulation necroses, especially in those removed from the rats.

Among the animals succumbing within two days of injection, decided congestion of the splenic pulp and numerous small thrombi of conglutinated erythrocytes in the vessels and sinuses were commonly found. At this time, more especially among animals surviving for longer periods, the pulp cords showed marked necrosis with some polymorphonuclear leukocytic infiltration and many megalokaryocytes.

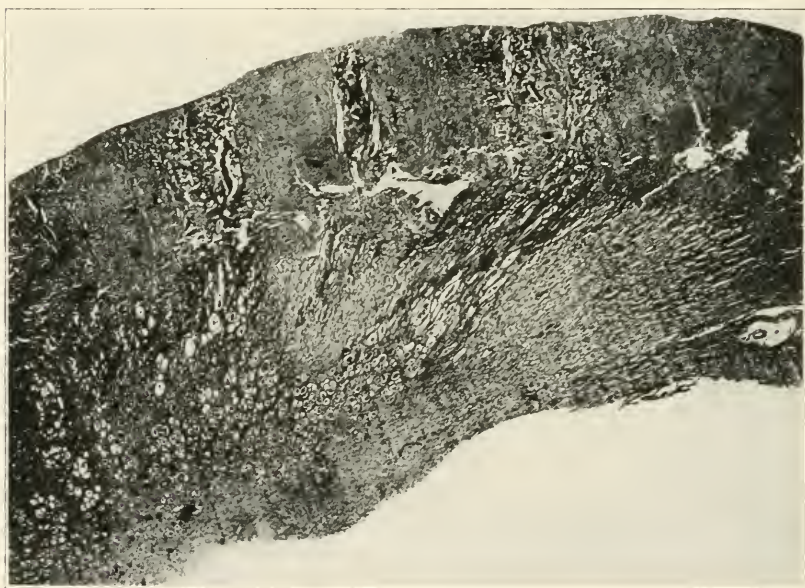


Fig. 13.—Kidney from rabbit injected with a single large dose of disodium arsphenamin; death eleven days after injection. Several large cortical patches are in a stage of partial necrosis, probably due to incomplete vascular occlusion (incomplete infarction). (Low dry lens magnification.)

These areas of coagulation necrosis were usually focal, small and distributed, but in some organs were quite large and had an almost hyaline and homogeneous appearance. Unusually large numbers of broken-down erythrocytes were seen; a fine homosiderin pigmentation was found.

As a general rule, the follicles were fairly well preserved and there was apparently no involvement of the trabecula and capsule.

HISTOLOGIC CHANGES PRODUCED BY INTRAVENOUS INJECTIONS
OF MULTIPLE SMALL THERAPEUTIC DOSES OF SOLUTIONS
OF DISODIUM ARSPHENAMIN

When a solution of arspenamin is neutralized with sufficient sodium hydroxid to just dissolve the precipitate and about one third more of this amount of alkali is added, a disodium compound results which is believed by some to be somewhat less toxic than solutions to which just enough alkali is added to dissolve the precipitate and "clear" the solution.

TABLE 5.—THE INTRAVENOUS INJECTION OF RATS WITH A SOLUTION OF DISODIUM ARSPHENAMIN EVERY THREE DAYS

Weight, Gm.	Sex	Dose per Kilo	2 Per Cent. Solution, C.c.	Number of Injec- tions
150	M	0.010	0.075	10
85	M	0.010	0.043	8
120	M	0.010	0.06	10
130	M	0.010	0.065	10
140	M	0.010	0.07	10
140	M	0.010	0.07	10

TABLE 6.—THE INTRAVENOUS INJECTION OF RABBITS WITH MULTIPLE DOSES OF A SOLUTION OF DISODIUM ARSPHENAMIN

Dose per kilo, 0.01 c.c.

	Weights on Day of Injection					
January 27.....	1,670	2,050	1,730	1,680	1,970	1,640
30.....	1,635	2,040	1,640	1,575	1,985	1,495
February 2.....	1,390	2,100	1,680	1,500	2,000	1,330
5.....	1,380	2,040	1,640	1,440	1,880	1,430
9.....	1,390	1,970	1,570	1,460	1,880	1,430
12.....	1,470	2,050	1,695	1,490	1,970	1,480
16.....	Exam.	Exam.	1,575	1,430	1,830	1,965
19.....	1,700	1,575	1,940	2,090
24.....	1,540	1,545	1,840	1,850
26.....	1,645	1,560	1,830	1,895
March 1.....	1,640	1,520	1,875	1,660
4.....	1,565	1,470	1,865	1,680
8.....	Exam.	Exam.	1,830	1,580
11.....	2,000	1,480
15.....	1,960	1,550
18.....	1,910	1,640
22.....	1,920	1,635
					Exam.	Exam.

A series of six rats were given from eight to ten intravenous injections of solutions of the disodium compound of arspenamin in doses of 0.01 gm. per kilogram of weight, corresponding to 0.6 gm. per 60 kilograms, which is the maximum dose usually administered at one time to human beings in the treatment of syphilis (Table 5); these animals were killed and necropsy examinations made about twenty-four hours after the last injection. The injections were given twice a week.

A series of six rabbits were given from six to eighteen injections of solutions of the disodium compound in the same amounts, namely, 0.01. gm. per kilo corresponding to 0.6 gm. per 60 kilos of weight, twice a week; animals were killed and necropsy examinations made after six, twelve and eighteen doses, as shown in Table 6.

The histologic examination of these tissues has proved of considerable interest, as the drug was administered in multiple small doses in a manner analogous to its administration to persons.



Fig. 14.—Kidney from rabbit injected with a single large dose of disodium arsphenamin (from rabbit whose kidney is shown in Figure 13). A portion of the cortex shows great tubular dilatation, tubular collapse, atrophy and degeneration of the lining epithelium. Many casts are present. (High dry lens magnification.)

Cerebrum, Cerebellum, Brain Stem and Meninges.—Inconspicuous changes were found. The meninges have generally shown a slight degree of hyperemia, but no cellular infiltrations; thrombi of conglutinated erythrocytes were generally absent, although a few such were found. Occasionally extravasated red cells were found. The vessels of the brain were slightly congested, and in some specimens slight perivascular edema was noted. The vascular endothelium sometimes appeared swollen. In sections of the brains of some of the rats, num-

erous irregularly distributed minute areas of focal hemorrhage were seen (Fig. 15), a few being surrounded by definite zones of early necrosis in which the cells were stained diffusely and indistinctly and the details of morphology obscured. These changes occurred particularly in animals that had received many injections.

Lungs.—The lungs of both series of animals have shown interesting and instructive changes. In specimens of animals receiving the maximum number of injections, the capillaries were tortuous and densely packed with erythrocytes, which sometimes were conglutinated. The walls of the air sacs were somewhat thickened and more cellular, due



Fig. 15.—Brain from rat injected with ten small doses of disodium arsenphenamin. A small focal hemorrhage is shown. (Low dry lens magnification.)

to proliferating fibrous tissue. In large areas the alveoli were filled with edematous fluid, in which hemosiderin-carrying phagocytes could here and there be seen. The whole picture suggested passive congestion of moderately long standing with diffuse capillary edema. In the animals receiving fewer injections, these alterations were less noticeable.

A few of the larger pulmonary vessels (of rabbits) contained partly conglutinated or hyalinized thrombi. In one animal which received six

injections a large vein was completely occluded by closely interwoven hyaline bands of whorl-like arrangement; calcium granules were scattered throughout this thrombotic mass. In another rabbit which had received the maximum number of injections an interesting thrombosis occluded four fifths of the large vein. This thrombus was in a stage of advanced organization, being composed of young connective tissue cells, between which was found a heavy deposit of calcium. A portion of this calcium was present in the form of coarse granules which were surrounded by syncytial giant cells; elsewhere the lime salts occurred in dense clumps. A new channel had formed lined by endothelium and containing well preserved red cells (Fig. 17).



Fig. 16.—Lung from rat injected with ten small doses of disodium arsphenamin; an area of bronchopneumonia with adjacent compensatory inflated lung tissue. A medium sized artery presents considerable thickening of its wall and narrowing of the lumen. (Low dry lens magnification.)

These thrombi probably illustrate a not infrequently occurring condition, namely, arsphenamin, even in small doses may occasion a few pulmonary clots, which, while not interfering with life, may produce some symptoms.

Some of the arteries exhibited slight proliferative endarteritis with swollen endothelium and proliferation of the subendothelial connective tissue, but in this connection it is well to remember that rabbits are prone to develop spontaneous arteriosclerosis.

The lungs of the rats exhibited the same kind of vascular changes but in a lesser degree; patches of bronchopneumonia were frequently found (Fig. 16). In these areas the bronchial walls were generally infiltrated with polymorphonuclear cells and the lumen filled with masses of degenerating leukocytes and cellular debris. The surrounding air sacs were almost entirely filled with leukocytes, a few erythro-



Fig. 17.—Large pulmonary vein from rabbit injected with seventeen small doses of disodium arspenamin. An organized thrombus fills about four-fifths of the lumen. A heavy calcium salt deposit is shown. A new channel relined with endothelium has formed. (High dry lens magnification.)

cytes and some desquamated epithelium or mixtures of edematous fluid and cells. In these areas of pneumonia, the alveolar walls were sometimes necrotic and infiltrated with polymorphonuclear leukocytes. In this connection it may be stated that both rats and rabbits, and par-

ticularly the former, are very susceptible to pulmonary infection. The animals having received the largest number of injections were particularly prone to exhibit inflammatory alterations.

In other areas free of pneumonia, the alveolar walls were prominent, their capillaries tortuous, often engorged and sometimes occluded by conglutinated red cells. Fibrous thickening of the alveolar walls, in a moderate degree, was found when the animals had received many injections.

The pleura showed no changes.

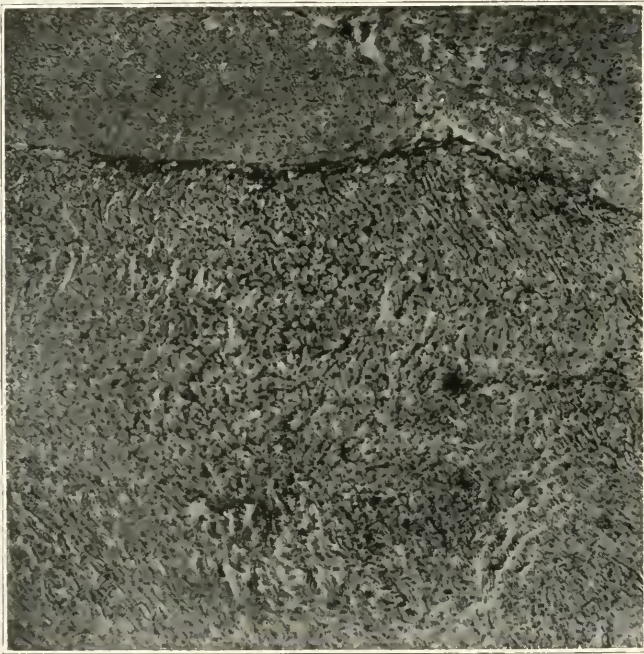


Fig. 18.—Heart from rat injected with ten small doses of disodium arsenophenamin. In a large part of the myocardium the muscle fibers are degenerated; between these fibers a fairly dense round cell infiltration exists. The degenerative and cellular infiltration appear sharply limited. (Very low magnification.)

Heart.—Sections of the hearts of some rats showed irregularly distributed focal areas of degeneration situated sometimes near the endocardium, sometimes beneath the epicardium or deep in the myocardium. The muscle degeneration in these areas was of various types, showing cloudy swollen fibers with indistinct or absent striations, homogeneous and hyalinized protoplasm and considerable vacuolization. Many of the muscle cells were mere broken-up structureless atrophic masses. In

these areas of focal necrosis were dense collections of large and small mononuclear cells with some fibroblasts and a few plasma cells; polymorphonuclear elements were inconspicuous. These areas of necrosis were evidently of different ages, as if some muscle degeneration had just begun, whereas in others degeneration was advanced and cellular infiltration quite extensive. Much variation as to size was present, but generally the areas of focal necrosis were quite small. In several instances they were so sharply limited as to suggest that only definite bundles were involved. This seemed to point toward infarction, or at least local anemia. Generally, the degree of tissue alteration stood in proportion to the medication received (Figs. 18 and 19).



Fig. 19.—Heart from rabbit injected with ten small doses of disodium arspenamin. This is a high magnification of a field shown in Figure 18. Between the degenerated muscle cells are large numbers of infiltrating small and large round cells. Polymorphonuclear leukocytes are rarely encountered in such areas.

The hearts of the rabbits also showed occasionally slight focal necrosis, but the changes were not so striking as in the hearts of the rats. Slight passive congestion, inconspicuous swelling of vascular endothelium, occasional small hyalinized thrombi and slight interstitial edema constituted the usual changes.

Liver.—Slight periportal fibrosis with small areas of focal necrosis, particularly in the peripheral portions of the lobules, constituted the most conspicuous changes in this organ.

The fibrosis was confined almost entirely to tissue about the blood vessels and bile ducts, and was never sufficiently extensive to surround a lobule.

The vascular changes were never great; a few thrombi of partly hyalinized masses of erythrocytes were found and only occasionally passive congestion of the intralobular veins. No changes were found in the bile ducts.

The areas of focal necrosis were found more especially in the rat's organs; these were quite small and generally in the peripheral portions

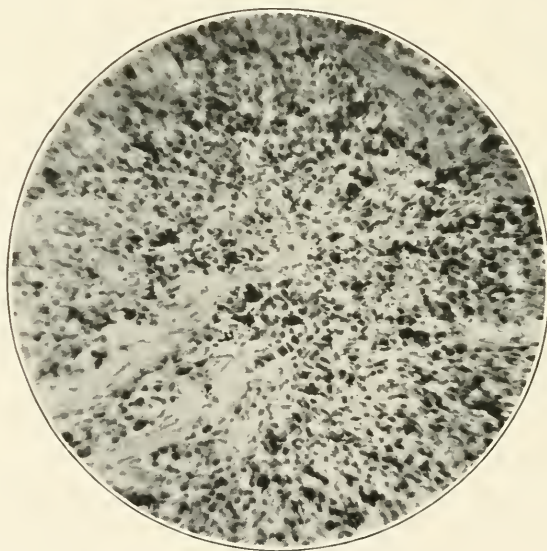


Fig. 20.—Spleen from rat injected with six small doses of disodium arsenamin. Many clumps of hemosiderin (black in photograph) are scattered throughout the tissue. In animals receiving the maximum number of injections the hemosiderin pigmentation is considerably more pronounced. (Low dry lens magnification.)

of the lobules, although this distribution was frequently very irregular. The appearance of these areas varied from groups of necrotic cells sometimes flooded with erythrocytes or areas of marked necrosis infiltrated with lymphocytes, to definitely fibrous round nodules in animals that had received the largest number of injections. The connective tissue proliferations were only discernible in the organs of those animals receiving the maximum number of injections.

Kidneys.—Vascular changes constituted the most prominent alterations embracing marked congestion, especially pronounced in the deeper cortical and outer boundary zones. The dilated vessels frequently contained thrombi of partially or entirely hyalinized masses of erythrocytes. The glomeruli, corpuseles and capsular spaces showed no abnormal changes, except that the vessels of the tufts were generally distended and frequently occluded with the hyalinized plugs of erythrocytes; collapsed glomerular capillaries were sometimes seen. Occasionally minute interstitial hemorrhages were found, likewise slight degrees of interstitial edema.

The tubules have usually shown minor changes generally confined to the convoluted tubules of the outer cortical zone and spiral portions of the outer boundary zone; the collecting tubules have shown no changes. In the involved areas the tubular cells have been found cloudy, swollen with granular and vacuolated protoplasm and degenerated nuclei. Here and there an inconspicuous connective tissue increase was encountered. This was seen only in animals receiving the maximum number of injections, and generally consisted of small groups of spindle cells or small round cells, generally situated about a glomerulus. Frank necrosis was not encountered. Evidences of cellular regeneration were frequently seen.

Suprarenals.—These organs have shown considerable variation among animals receiving the same amounts of arspenamin per body weight at the same time and examined by necropsy at the same intervals after injection. In all instances the suprarenals were removed and fixed within an hour after death.

In the animals receiving the smaller number of injections a definite increase in size and quantity of the cortical lipoid was observed. All three zones of the cortex exhibited this lipoid increase, but the middle zone was the seat of the greatest accumulation. In the animals receiving the largest number of injections a slight lipoid exhaustion was present, particularly affecting the outer zone.

There appeared to be a distinct swelling of the cortical cells, and frequently many cells were seemingly regenerating.

The vascular changes were slight, the capillaries being occasionally engorged with conglutinated or hyalinized masses of red cells. The larger vessels showed no alterations. There was no change in the interstitial substance.

In the medullary portions many of the cells were shrunken, and while most contained some chromaffin, there were many that did not, and we are of the opinion that the majority of sections showed slight chromaffin depletion.

Spleen.—The principal change was one of passive congestion with slight hemosiderosis and fibrillar fibrosis, particularly in the animals receiving the maximum number of injections (Fig. 20). The capsule and trabeculae showed no structural changes, or at most slight fibrosis in those animals receiving ten or more injections. A few giant cells resembling megalokaryocytes were occasionally encountered, and the malpighian follicles were generally rather large, with prominent germinal centers.

SUMMARY AND DISCUSSION

It is to be emphasized that considerable individual variations in the histopathologic changes were found in the various organs of animals receiving the same drug under similar experimental conditions; general changes may be summarized as follows:

1. *Changes Produced by Acid Solutions of Arsphenamin.*—1. The blood vessels of the organ examined (brain and meninges, lungs, heart, liver, spleen, kidney and suprarenal) were either intensely engorged or occluded by thrombi consisting of partly or entirely conglutinated or hyalinized erythrocytes.

2. This thrombosis was irregularly distributed.

3. In the larger pulmonary vessels and in the distended chambers of the right side of the heart the thrombi were a peculiar light yellow-green, and consisted of homogeneous bands arranged in whorl-like formation ("acid-arsphenamin thrombi").

4. Occasional small capillary hemorrhages were found.

5. There were no tissue alterations (death having occurred immediately after injection), excepting in one animal which survived for five hours and which exhibited early parenchymatous degeneration, particularly in the liver and kidney.

2. *Changes Produced by Single Large Doses of Solutions of Disodium Arsphenamin (0.100 gm. per kilo or 6 gm. per 60 kilos).*—1. The tissue alterations were prominent and depended chiefly on the number of days the animal survived the injection.

2. Degenerative tissue changes predominated over the vascular changes. In the liver unevenly distributed areas of necrosis, often of extreme extent, were seen. The kidneys exhibited extensive tubular necrosis and calcium deposition; the spleen often presented irregular areas of coagulation necrosis; in the suprarenals there was a depletion of the lipid and chromaffin contents. Areas of focal necrosis were found in the myocardium. The brain tissue was little altered.

3. The vascular changes consisted of more or less pronounced congestion and irregularly distributed conglutination and hyaline thrombi;

these may be in part responsible for the degenerative changes. Small focal hemorrhages were frequently found.

4. These changes were produced by arspphenamin prepared by three different laboratories.

3. *Changes Produced by Multiple Small Doses of Solution of Disodium Arspphenamin (0.01 gm. per kilo or 0.6 gm. per 60 kilos).*—1. The lesions in these series were inconspicuous and varied according to individual susceptibility and the number of doses injected.

2. A very slight connective tissue proliferation was found in the lung, liver, spleen and kidney of the animals receiving the maximum number of injections.

3. More or less marked chronic passive congestion was found with moderate hemosiderosis in the spleen; inconspicuous amounts of hemosiderin occurred in the lung.

4. Occasional vessels contained thrombi composed of partly or entirely conglutinated or hyalinized erythrocytes. In the lung of two animals organized thrombi were found.

5. Areas of bronchopneumonia, of doubtful origin, were encountered.

6. Areas of focal necrosis, inconspicuous in the heart and more pronounced in the liver, were seen.

7. The lipoids of the suprarenals were at first increased in quantity; later a slight exhaustion appeared. An ill-defined chromaffin exhaustion took place.

8. Parenchymatous changes of mild degree were seen, but these were never of such degree as to interfere with the function of the various organs.

9. These changes were produced by arspphenamin prepared by three different laboratories.

In general it would appear that the primary changes produced by arspphenamin are vascular in nature and consist of more or less marked congestion and the production of numerous thrombi by conglutination of erythrocytes, which later may become more or less hyalinized.

These vascular phenomena have been found in varying degree in all of the organs examined and have been most severe after the intravenous injection of acid solutions of arspphenamin, and much less evident after the administration of the alkaline or disodium solution.

The constitution of the thrombi are especially interesting in view of the theory of Danysz,⁶ that carbon dioxid and sodium biocarbonate

6. Danysz, W.: Ann. d. l'Inst. Pasteur **31**:114, 1917.

of the blood change arsphenamin into an insoluble base with the production of emboli or precipitates, which later may be dissolved in part or entirely by the leukocytes and organic bases of the plasma; also in view of the theory of Berman,⁷ that an increase of the globulin fraction of the serum proteins in certain persons may result in their precipitation in vivo. In studies on these subjects previously referred to⁸ the conclusion was reached that the theory of Danysz may be accepted as explaining in part the reactions caused by the intravenous injection of acid solutions of arsphenamin, to a lesser extent of concentrated monosodium solutions, but not at all of solutions of disodium arsphenamin, because of the negative character of all tests with the latter solutions.

As shown in the present studies, thrombi were found in practically all organs after the administration of solutions of acid and disodium arsphenamin; these thrombi were readily recognized as conglutinated masses of erythrocytes which later became hyalinized, due in part to hemolysis and autolysis. The characteristic and peculiar whorl-like construction and color of these masses caused by the administration of acid solutions indicates that they may have been composed of precipitates in addition to hemolyzing erythrocytes; the same is probably true of the thrombi found after the administration of single large doses of solutions of disodium arsphenamin and to a lesser extent of those thrombi caused by the intravenous injection of multiple small doses of disodium arsphenamin. The relation of hemolysis to these intravascular phenomena is especially significant as arsphenamin itself is hemolytic, especially acid and disodium solutions in water.⁹

Next to the vascular phenomena, varying degrees of degeneration and necrosis in parenchymatous organs were frequently conspicuous, especially among those animals surviving large amounts of arsphenamin for a sufficient time for necrotic changes to occur. Areas of necrosis of muscle cells were found in the heart; islands of necrotic liver and spleen were frequently conspicuous and pronounced nephrosis commonly occurred. While a portion of these degenerative and necrotic changes may reasonably be ascribed to the effects of thrombosis and embolism, one cannot escape the conclusion that solutions of arspen-

7. Berman, W.: The Nitritoid Crisis after Arsphenamin Injections, *Arch. Int. Med.* **22**:217, 1918.

8. Schamberg, J. F.; Kolmer, J. A.; Raiziss, G. W., and Weiss, C.: Laboratory and Clinical Studies Bearing on the Causes of the Reactions Following Intravenous Injections of Arsphenamin and Neo-Arsphenamin, *Arch. Dermat. & Syph.* **38**:235-256, 1920.

9. Kolmer, J. A., and Yagle, E. M.: Hemolytic Activity of Solutions of Arsphenamin and Neo-Arsphenamin, *J. A. M. A.* **74**:643 (March 6) 1920.

amin are capable of direct tissue injury of varying severity, according to the size of the dose, nature of the solution and to some extent of the species of animal.

The suprarenal changes of congestion and thrombosis, cellular degenerations and reduction in lipoid and chromaffin contents are particularly significant and indicate the important relation of suprarenal injury to arsphenamin therapy and the possibility of a relation between changes in this organ and certain symptoms following at times the administration of this drug to human subjects. By reason of the practical importance of this subject, we are continuing this study by means of combined histologic and biochemical investigations.

It is to be emphasized that the maximum changes were produced by large doses of acid or nonneutralized solutions of arsphenamin and by doses of solutions of disodium arsphenamin from eight to twelve times greater than the largest single dose commonly administered to human beings at one time; also that the administration of multiple small doses analogous to those given in the treatment of syphilis, produced at the most such slight tissue changes as would not in all probability influence the function of the various organs. The latter naturally possess a greater practical significance and interest. As previously stated, these histopathologic changes have been produced in these experiments by arsphenamin from three different laboratories; no differences were discernible in the effects according to the particular brand of arsphenamin employed. The researches of Ullmann¹⁰ indicate that the prewar salvarsan of German manufacture produced lesions of similar kind and degree as those found by us and described in this report.

CONCLUSIONS

1. The intravenous injection of lethal doses of acid non-neutralized solutions of arsphenamin in experimental animals produces widespread and severe vascular injury characterized by congestion, thrombus formation and hemorrhage; later cellular degeneration and necrosis take place.
2. The intravenous injection of single large doses of solutions of disodium arsphenamin (ten times larger than the maximum amount administered to human beings at one time) produce severe vascular and tissue alterations, particularly in the liver, kidney, suprarenals and spleen.
3. The intravenous injections of multiple therapeutic doses of solutions of disodium arsphenamin corresponding to doses of 0.6 gm. per

10. Ullmann, K.: Experimentelles zur arsenwirkung auf die organe, Wien. klin. Wchnschr. **27**:838-843, 1914.

60 kilos of body weight, produce inconspicuous tissue alterations that do not appear to be sufficiently pronounced to interfere with the functions of the organs.

4. Detailed descriptions of the histologic changes found in the brain and meninges, heart, lungs, liver, kidneys, suprarenals and spleen are given.

5. These changes were induced by arsphenamin prepared by several different laboratories.

6. These histopathologic changes probably bear an important relation to arsphenamin reactions and to methods of arsphenamin therapy.

A STUDY OF THE HISTOLOGIC CHANGES PRODUCED EXPERIMENTALLY IN RABBITS
BY NEO-ARSPHENAMIN *

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In the preceding article,¹ we have summarized the histologic changes found in certain organs of rats and rabbits at varying intervals after the intravenous injection of solutions of arsphenamin in single large and multiple therapeutic doses. The purpose of the present article is to record the results of a similar study with solutions of neo-arsphenamin.

This study has proved of much interest not only in relation to the subject of chemotherapy with arsenic compounds, but particularly by reason of its bearing on the choice of arsphenamin or neo-arsphenamin for the treatment of syphilis. As shown by Schamberg, Kolmer and Raiziss,² neo-arsphenamin injected intravenously is generally borne by white rats in a dose of 0.254 gm. per kilo of body weight and arsphenamin in a dose of about 0.105 gm. per kilo, the latter being more than twice as toxic as the former for this animal under identical conditions.

EXPERIMENTAL

White rats and rabbits were employed in all experiments. Neo-arsphenamin was administered to rats by injection into the saphenous vein with a gravity apparatus, in the form of 4 per cent. solutions in

*From the Dermatological Research Laboratories of Philadelphia and the McManes Laboratory of Pathology of the University of Pennsylvania.

*Investigations aided by funds accruing from the preparation of neo-arsphenamin.

1. Kolmer, J. A., and Lucke, B.: An Experimental Study of the Histologic Changes Produced Experimentally in Rabbits by Arsphenamin, *Arch. Dermat. & Syph.*, this issue, p. 483.

2. Schamberg, J. F.; Kolmer, J. A., and Raiziss, G. W.: A Comparative Study of the Toxicity of Arsphenamin and Neo-Arsphenamin, *Am. J. M. Sc.* **160**:188, 1920.

freshly distilled water at the rate of 0.5 c.c. per minute; rabbits were injected by means of a syringe into an ear vein.

The majority of animals were killed at chosen intervals by a brief exposure to illuminating gas and the necropsy examinations performed at once; the remaining animals were usually examined within twelve hours after death. As described in our paper concerning the histopathologic changes produced by arsphenamin,¹ a brief (stupefying) exposure to illuminating gas did not produce any discernible tissue changes as determined by histologic studies conducted with a number of control animals, including both rats and rabbits.

The following organs were removed and divided into two parts and placed in Orth's fluid, and in 5 per cent. neutral formaldehyd: cerebrum, cerebellum, brain stem and meninges; heart, lungs, liver, kidneys, suprarenals and spleen. Paraffin and frozen sections were prepared from different parts of the organs and stained with hematoxylin and eosin. Special studies were made of the suprarenals in reference to the chromaffin cells and also of the lipoid contents, frozen sections being stained with Herxheimer's scharlach r for the latter.

RESULTS

HISTOLOGIC CHANGES PRODUCED BY SINGLE MASSIVE DOSES OF NEO-ARSPHENAMIN

In determining the toxicity of neo-arsphenamin, white rats weighing from 100 to 150 gm. were injected intravenously with 0.200 gm. per kilo of body weight in 4 per cent. solutions in distilled water at the rate of 0.5 c.c. per minute; this dose corresponds to 12 gm. per 60 kilos, and 60 per cent. of the animals must survive at least seven days to pass the official Hygienic Laboratory test. Seven animals succumbing at varying intervals during these routine tests over twenty different lots of neo-arsphenamin have been examined histologically and included in this study; the duration of life of each of the seven animals chosen are shown in Table 1.

TABLE 1.—THE INTRAVENOUS INJECTION OF RATS WITH SINGLE LARGE DOSES OF NEO-ARSPHENAMIN

Weight, Gm.	Sex	Dose per Kilo	Results
100	M	0.200	Lived one day
110	M	0.200	Lived two days
100	M	0.200	Lived five days
135	F	0.200	Lived six days
120	M	0.200	Lived eight days
150	M	0.200	Lived nine days
120	M	0.200	Lived twelve days

Rabbits were also given intravenous injections of 0.200 gm. of neo-arsphenamin per kilo of body weight, dissolved in 10 c.c. of sterile distilled water; this dose corresponds to 12 gm. per 60 kilos of body

weight and is approximately fourteen times greater than the average dose given to human beings at one time in the treatment of syphilis. The animals were killed at varying intervals, as shown in Table 2, and the tissues examined histologically.

TABLE 2.—THE INTRAVENOUS INJECTION OF RABBITS WITH SINGLE LARGE DOSES OF NEO-ARSPHENAMIN

Weight, Gm.	Dose per Kilo in 10 C.c.	Results
1,880	0.200	Examined 3 days after injection
1,850	0.200	Examined 5 days after injection
1,610	0.200	Examined 7 days after injection
1,650	0.200	Examined 12 days after injection

A histologic examination of these tissues has shown the following changes:

Cerebrum, Cerebellum, Brain Stem and Meninges.—Among the animals succumbing within two days after the injection, congestion of the vessels of the pia and to a lesser extent of brain tissue was found. In many of these vessels the erythrocytes were conglomerated or partly hyalinized. A slight degree of perivascular and periganglionic edema was occasionally present. Numerous small hemorrhages in the substance of the brain were also seen, more especially in the brains of rats.

Among animals of both species surviving these periods of time, no changes at all were found, except more or less congestion and an occasional minute hemorrhage. The brain substance showed no discoverable alterations.

Lungs.—Among the animals succumbing within two days after injection, the lungs have shown congestion of marked degree and a few scattered thrombi of conglomerated erythrocytes. The congested capillaries rendered the alveolar walls prominent, but edema and hemorrhagic extravasation into the interstitial tissue and sacs were only exceptionally found.

Among animals surviving for longer periods, slight congestion of the capillaries was seen with inconspicuous mononuclear infiltration of the alveolar walls. The congestion became less extensive in proportion to the number of days the animal survived the injection. In three of the rabbits a peculiar sclerosis of the larger arteries was noted with considerable proliferation of the intima, which narrowed the lumen to a considerable degree. An organizing thrombus was found in one artery. Occasionally areas of pneumonitis were encountered; these were probably not produced by the medication, being commonly found in experimental rats and rabbits.

The pleura showed no changes.

Heart.—Among the animals succumbing within one or two days after injection, great congestion with slight edema, conglutination of the erythrocytes and an occasional small hemorrhage constituted the important changes.

Among animals surviving for longer periods similar but less marked vascular changes were found, but occasional areas of focal degeneration of the muscle were encountered. In these areas the muscle cells appeared smooth and even vacuolated and had degenerated nuclei. Between the involved muscle fibers fairly dense accumulations of small and large round cells were seen. These changes were conspicuous in only two animals.

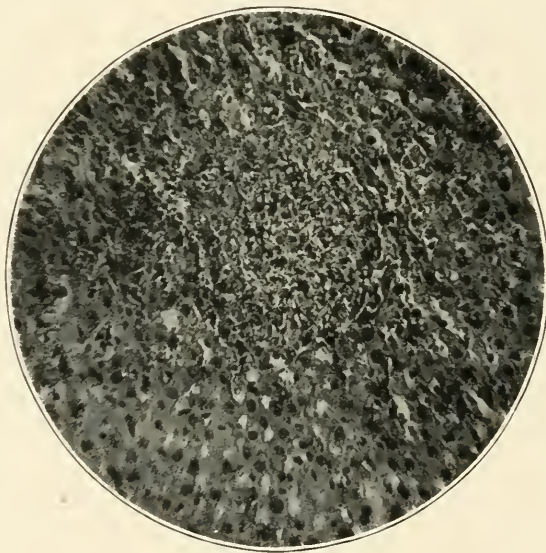


Fig. 1.—Liver from rat injected with a single large dose of neo-arsphenamin; death six days after injection. A small area of focal necrosis is shown. Numerous such areas were present. (Low dry lens magnification.)

Liver.—Among the animals succumbing within a day or two of injection marked congestion of the intralobular veins, and the presence of numerous thrombi composed of conglutinated and partly hyalinized erythrocytes constituted the most conspicuous lesions. Associated with this hyperemia was a slight degree of cloudy swelling of the liver cells, particularly in the central lobular areas. Many of the cells in these regions possessed a coarsely granular or irregularly vacuolated protoplasm, while little nuclear changes were seen.

Among animals surviving for five days or longer, congestion and small thrombi were likewise found, but a more prominent change

embraced numerous small areas of necrosis irregularly distributed in the lobules, and apparently not occurring in any constant lobular zone. These areas were rounded and involved approximately only from 30 to 40 hepatic cells (Fig. 1.). They stained rather lightly with eosin, were usually granular but sometimes quite smooth and homogeneous, and were occasionally flooded with red blood corpuscles. Slight leukocytic infiltration was occasionally noted in these areas; this was more pronounced in animals that survived over ten days.

The periportal tissues showed no constant changes; the bile ducts appeared unchanged.

Kidneys.—These have usually shown profound changes, the kind and severity depending on the duration of life after the injection of

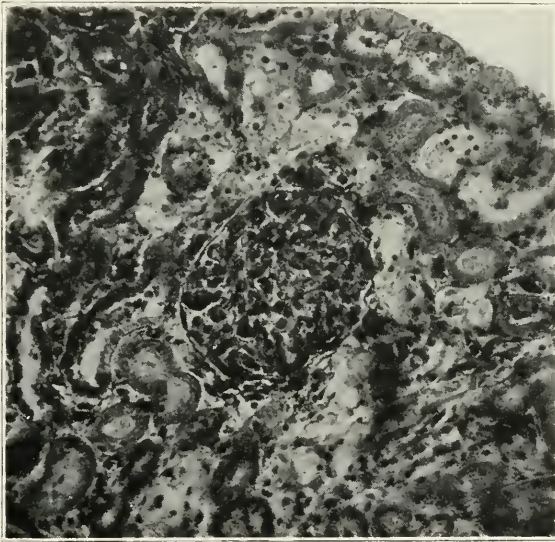


Fig. 2.—Kidney from rat injected with a single large dose of neo-arsphenamin; death after twenty-four hours. The capillary loops of the glomerular tuft shown are widely distended and occluded with conglutinated and partly hyalinized erythrocytes. Many of the convoluted tubules possess degenerated, often frankly necrotic, epithelial lining; the tubular lumen contains granular albuminous debris. (High dry lens magnification.)

the drug. As a general rule, the changes occurring in the kidneys of rats and rabbits were similar, but were greater in the former.

Among animals succumbing within one and two days after injection, vascular changes were most prominent. The glomeruli were large, the capillary tufts being distended, their component capillaries containing numerous thrombi of conglutinated and hyalinized erythrocytes (Fig. 2). The capillary endothelium was often swollen, stained poorly and

apparently was undergoing degeneration. The capsules of Bowman showed no change other than slight swelling of the lining cells; the capsular spaces were either completely filled by the distended tufts or else contained small amounts of edematous fluid. Congestion was most profound in the boundary zone, and numerous small hemorrhages were widely distributed; slight intertubular edema was found. Conglutination and hyalinization of erythrocytes were everywhere present. The epithelium of the convoluted tubules, particularly in the outer cortex, was swollen, granular, often completely necrotic and desquamated. Hyaline droplets were often seen, and frequently casts obstructed the various tubules.

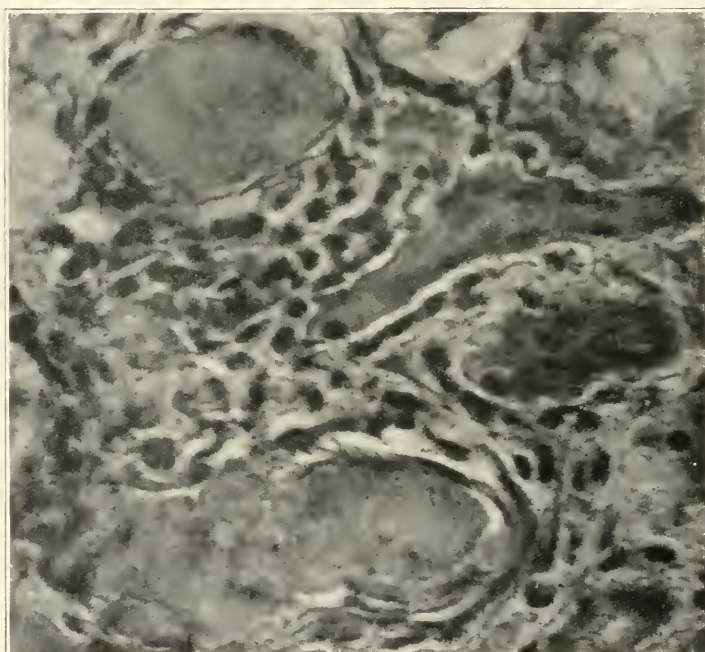


Fig. 3.—Kidney from rat injected with a single large dose of neo-arsphenamin; death after six days. Necrosis of lining epithelium of convoluted tubules. (High dry lens magnification.)

Within forty-eight hours of the time of injection profound tubular changes were apparent; many of the convoluted tubules especially showed frankly necrotic epithelium contrasting sharply with the well preserved lining of the collecting tubules. Hyaline droplets were frequently found in the tubules; likewise granular debris and erythrocytes. Vascular changes were still prominent and similar to those already mentioned.

Among animals surviving three to four days the vascular changes were less prominent but were still conspicuous; tubular necrosis was even more pronounced, especially in the convoluted portions.

Among animals surviving five or six days, hyperemia was less marked but numerous hemorrhages were found throughout.

The glomeruli were generally small with shrunken and often fragmented tufts; the capsular spaces were frequently filled with cellular debris, and the lining cells of the capsule were somewhat swollen.

Tubular necrosis was especially severe, and practically none of the tubules in the cortex escaped; the convoluted portions especially were

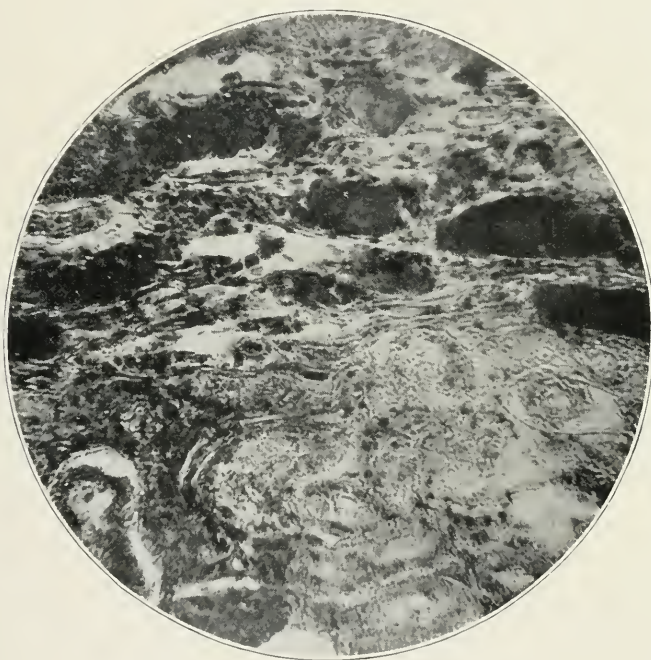


Fig. 4.—Kidney from rat injected with a single large dose of neo-arsphenamin; death six days after injection. Frank tubular necrosis; deposition of calcium salt (black in photograph) in necrotic cells of some tubules. (High dry lens magnification.)

so necrotic that even the basement membranes were indistinct. A large degree of calcium infiltration was found in the necrotic portions, the earliest deposit being near the basement membranes of the involved tubules (Figs. 3 and 4).

Among animals surviving nine days or longer, slight congestion was found and patchy rather than generalized tubular necrosis, with evidence of beginning repair.

Suprarenals.—Among the animals succumbing within one or five days, pronounced depletion of both lipid granules and chromaffin were seen; among animals surviving over ten days there were great variations in histologic appearances but with an apparent tendency toward restoration of lipid and chromaffin. Considerable congestion of the medullary portions were seen in animals dying after a few days. Slight necrosis of the cells of the middle zone of the cortex was found in several animals surviving five days or longer.

Spleen.—Among the animals succumbing within two days, congestion and numerous thrombi of conglutinated erythrocytes were seen. Among animals surviving longer intervals there was less hyperemia, but considerable hemosiderin was found both free and in large phagocytic cells. Occasionally areas of pulp necrosis were found flooded with erythrocytes. In animals surviving ten days or longer there were evidences of proliferation of the fibrous tissue reticulum, probably due to passive congestion. Many megalokaryocytes were encountered.

HISTOLOGIC CHANGES PRODUCED BY MULTIPLE THERAPEUTIC DOSES OF NEO-ARSPHENAMIN

Rats were given from five to ten intravenous injections of neo-arsphenamin in the form of 1 per cent. solutions in distilled water in doses of 0.020 gm. per kilo of body weight every three or four days; this dose corresponds to 1.2 gm. per 60 kilos, which is slightly greater than the amount usually administered to human beings at one time, namely, 0.9 gm. Table 3 shows the number of injections given.

TABLE 3.—THE INTRAVENOUS INJECTION OF RATS WITH SOLUTIONS OF
NEO-ARSPHENAMIN EVERY THREE DAYS

Weight, Gm.	Sex	Dose per Kilo	Injections
120	Male	0.020	10
110	Female	0.020	10
95	Male	0.020	10
95	Female	0.020	10
130	Male	0.020	6
130	Male	0.020	3

Rabbits were given from five to eighteen intravenous injections of neo-arsphenamin at intervals of three to four days in a dose of 0.030 gm. per kilo dissolved in 5 c.c. of sterile distilled water; this dose corresponds to 1.8 gm. per 60 kilos, which is double the maximum amount administered to human beings at one time. Table 4 shows the number of injections given and the influence on body weight.

The following histologic changes were found:

Cerebrum, Cerebellum and Meninges.—The only noteworthy changes were a slight degree of passive congestion of the pia with a

few small thrombi of conglutinated erythrocytes; occasionally small areas of hemorrhagic extravasation in the meninges were encountered.

The vessels in the brain substance were likewise occasionally engorged and surrounded with edematous zones; there were no evidences of leukocytic infiltration or noteworthy changes in the ganglionic cells.

TABLE 4.—THE INTRAVENOUS INJECTION OF RABBITS WITH MULTIPLE DOSES OF NEO-ARSPHENAMIN

Dose per kilo, 0.030 C.c.

		Weight on Days of Injection					
January	24.....	1,950	2,200	2,110	2,065	1,890	1,790
	27.....	2,100	2,090	1,870	1,920	1,745	1,590
	30.....	2,055	2,070	1,815	1,865	1,760	1,655
February	2.....	1,930	2,075	1,680	1,785	1,725	1,530
	5.....	1,970	1,990	1,610	1,750	1,690	1,520
	9.....	2,040	2,090	1,595	1,740	1,770	1,590
	12.....	Exam.	Exam.	1,730	1,890	1,860	1,630
	16.....	1,650	1,690	1,750	1,550
	19.....	1,655	1,440	1,740	1,655
	24.....	1,640	Exam.	1,700	1,595
	26.....	1,560	1,840	1,640
March	1.....	Exam.	1,740	1,660
	4.....	1,730	1,575
	5.....	1,620	1,440
	11.....	1,670	1,320
	15.....	Exam.	1,500
	18.....	1,695
	22.....	1,775
	24.....	Exam.

Lungs.—In the animals receiving the maximum number of injections passive congestion with early fibrosis constituted the principal changes. Occasionally the congested capillaries contained small masses of hyalinized red blood corpuscles. The alveolar walls were generally slightly thickened, their capillaries tortuous and protruding into the air sacs as budlike projections. Small areas were found to be collapsed and the neighboring regions frequently showed distended sacs of compensatory emphysema.

Some of the larger arteries presented slight evidences of proliferating endarteritis with partial obliteration of their lumena; others have shown changes in the cells of the mesial coat with nuclear degenerations. These lesions are probably "spontaneous."

The pleura and bronchi have shown no changes.

Heart.—Lesions were frequently encountered, especially among the rats. The changes were in the nature of irregularly distributed minute focal or patchy areas of atrophy or degeneration of muscle cells with mononuclear cell infiltration. In one such area, measuring about 300 microns in diameter, bluish granular material was found in the necrotic muscle cells closely resembling calcium infiltration, such as is known to occur in degenerated heart muscle.

Aside from these areas of focal necrosis, the vessels were frequently congested and occasionally contained thrombi of conglutinated erythrocytes; in some instances the lining endothelium of the arteries appeared swollen.

Liver.—Among the rats changes were usually found in the nature of multiple foci of necrosis; among the rabbits these changes were much less pronounced.

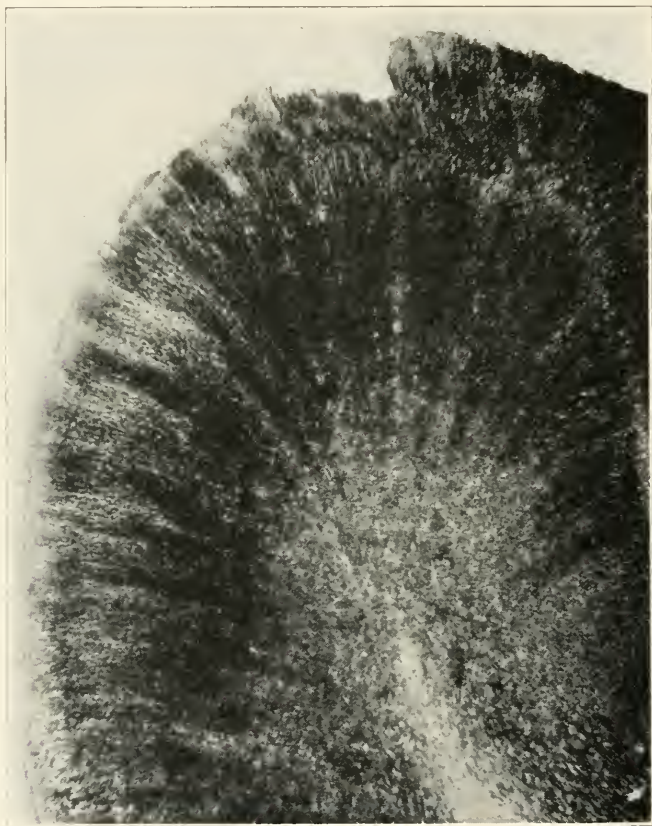


Fig. 5.—Suprarenal from rabbit injected with six small doses of neo-arsphenamin. The cortical lipoids (stained with scharlach r; black in photograph) are greatly increased in quantity, all the cortical zones containing considerable excess. (Dry low power magnification.)

As a general rule, the necrotic areas involved only a portion of a lobule and were irregularly located; occasionally, however, a necrotic area involved groups of lobules. These areas were generally of a rounded shape and consisted of a granular pinkish detritus with fatty vacuoles and nuclei in various stages of necrosis. Frequently a well

marked leukocytic infiltration was seen with beginning fibrous tissue repair, which gave these areas a cellular appearance.

In the perilobular tissues the bile ducts presented no great alterations from the normal; the vessels, however, usually showed some hyperemia and the surrounding tissues presented slight mononuclear infiltration with inconspicuous fibrosis.

Kidneys.—The changes in both rats and rabbits were generally mixed vascular and tubular in type and of a mild rather than severe degree.

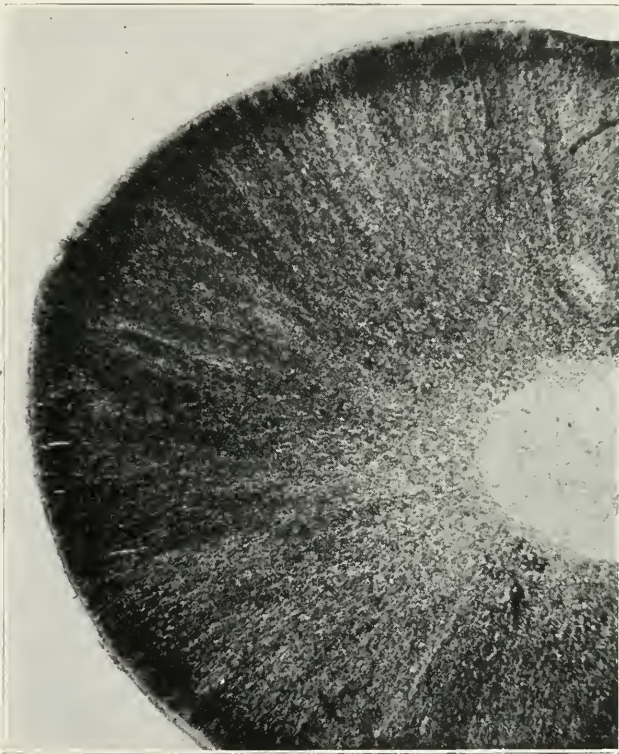


Fig. 6.—Suprarenal from rabbit injected with eleven small doses of neo-arsphenamin. The cortical lipoids (stained with scharlach r; black in photograph) are somewhat reduced in quantity, the reduction being more pronounced in the inner cortical zones. The zona glomerula still contained an excess of lipid material. (Very low magnification.)

The capillaries of the glomeruli were generally moderately distended, as were likewise the vessels in the boundary zone. The capsules showed no changes other than occasionally a slight proliferation of the lining cells; proliferation of the glomerular endothelium also occurred giving the tufts a more cellular appearance. This occurred

particularly in the animals receiving the maximum injections. Small interstitial hemorrhages were sometimes seen.

The parenchymatous changes were principally in the nature of cloudy swelling of the epithelial cells of the convoluted tubules; slight vacuolization and desquamation were occasionally seen. A few tubules contained casts of albuminous material and masses of erythrocytes. Definite necrotic changes were never seen.

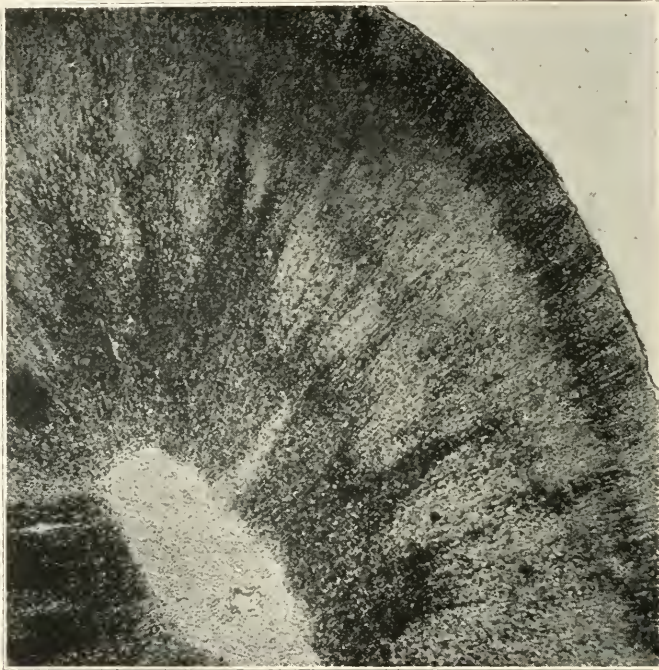


Fig. 7.—Suprarenal from rabbit injected with fifteen small doses of neoarsphenamin. The cortical lipoids (stained with scharlach r; black in photograph) are greatly reduced in quantity, the reduction being more apparent in the zona fascicularis. (Very low power magnification.)

Suprarenals.—These organs have not shown pronounced changes. Generally some passive congestion was found in the medullary portions.

In the animals which received few injections a pronounced increase in the size, as well as the amount, of the cortical lipoids was found (Fig. 5); in animals receiving a large number of injections a gradual lipid depletion was observed (Fig. 6). This depletion was generally great when the maximum number of doses were given (Fig. 7).

In some animals there appeared to be a decrease of chromaffin; in others an increase, and in others a normal amount, as compared with the controls.

Spleen.—The principal changes were passive congestion, hemosiderosis and early fibrillar fibrosis (Fig. 8). Areas of pulp were flooded with poorly outlined erythrocytes, and the sinuses frequently showed swollen endothelial cells and numerous phagocytes, carrying erythrocytic fragments and pigment.

Among the animals receiving ten or more injections, the splenic reticulum and the walls of veins were somewhat more prominent.

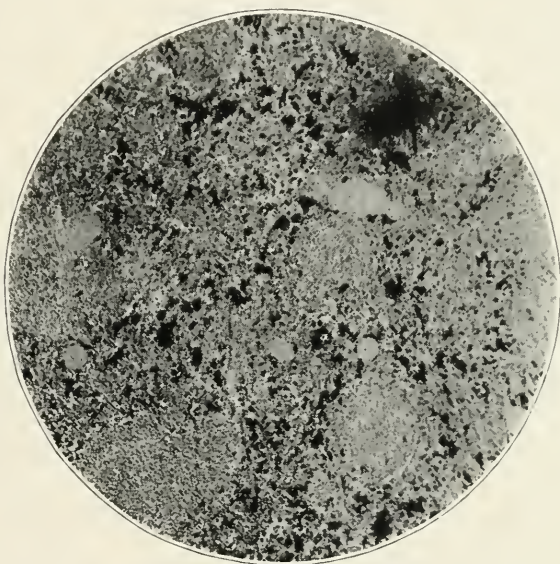


Fig. 8.—Spleen from rabbit injected with fifteen doses of neo-arsphenamin. Considerable quantities of hemosiderin occurring in thick clumps, as well as fine granules, are present (stained black in photograph). The large round areas are splenic follicles out of focus. (Low dry lens magnification.)

SUMMARY AND DISCUSSION

While considerable variation was found in the degree of histopathologic changes occurring in the various organs of individual animals, the changes in rats and rabbits were similar and may be briefly summarized thus:

Changes Produced by the Intravenous Injections of Single Massive Doses of Neo-arsphenamin (0.200 per Kilo or 12 gm. per 60 Kilos Being About Fourteen Times the Average Human Dose).—1. The tissue alterations varied with the number of days the animals survived

the injections, being most pronounced in those which lived for five or more days.

2. Degenerative changes predominated over the vascular changes. In the liver cellular degeneration and irregularly distributed focal necrosis were found. There was marked renal necrosis with deposition of calcium; occasional areas of focal necrosis were found in the heart and the spleen. In the suprarenal alterations in lipoid and chromaffin contents were marked.

3. Vascular changes occurred, particularly in animals dying within a few days, more or less congestion and thrombosis being present. Occasional capillary hemorrhages were found.

4. These changes were produced by neo-arsphenamin prepared by several different laboratories.

Changes Produced by the Intravenous Injection of Multiple Small Doses of Neo-arsphenamin (0.02 to 0.03 per Kilo Equivalent to 1.2 to 1.8 gm. per 60 Kilos Being Two to Three Times the Amount Administered to Human Beings at One Time).—1. The lesions in this series were slight, and were least in those animals that received the fewest number of injections.

2. A slight connective tissue proliferation was found in the lungs, spleen and liver of the animals receiving the largest number of injections.

3. More or less chronic passive congestion was observed; moderate hemosiderosis was present in the spleen.

4. Occasional vessels were occluded with conglutination or hyaline thrombi.

5. Small areas of focal necrosis and cellular infiltration were found in the heart and the liver.

6. Alterations of the suprarenal lipoids and chromaffin were seen.

7. Parenchymatous tissue changes were of mild degree and never of such type as would presumably interfere with the function of the organ.

8. These changes were produced by neo-arsphenamin prepared by several different laboratories.

Comparison with similar studies made with arsphenamin² have shown that massive single and multiple small doses of neo-arsphenamin produce histopathologic changes in the various organs of rats and rabbits to those produced by arsphenamin, but of lesser severity.

The vascular changes are similar but less extensive: Thrombi were found, but their production is more difficult to explain. Neo-arsphenamin in contradistinction to arsphenamin is not hemolytic in vitro, although solutions in water may be hemolytic unless prepared in such

a manner as results in isotonicity.³ Precipitates do not usually form *in vitro* when solutions of neo-arsphenamin are added to serum proteins or to solutions of various salts as bicarbonates and phosphates. Danysz has stated that novarsenobenzol (neo-arsphenamin) is only precipitated in the blood stream under exceptional circumstances when the amount of phosphates in the blood is much higher than normal. The thrombi are composed of conglutinated erythrocytes which later assume a smooth hyaline appearance, but the cause of their production by the intravenous injection of solutions of neo-arsphenamin is not clear; hemolysis probably played some part as the solutions used in these experiments were not isotonic.

The cellular degenerations and necrosis found in the heart, liver and kidneys were similar to those found in the arsphenamin series, but usually of lesser degree.

It is to be emphasized, as in the preceding article, that these lesions were produced by relatively large doses of neo-arsphenamin from three different manufacturers, and it is hoped that the results will not create a false or unfavorable impression of the drug; the important practical deductions to be drawn from these studies, aside from their relation to the general subject of chemotherapy with arsenical compounds are, that in relation to dosage, neo-arsphenamin is less likely to produce tissue injury than arsphenamin, but that more information is desirable and necessary on the questions of dosage and elimination of both compounds, so that either may be employed in the treatment of disease with least possibility of producing injury.

From the standpoint of tissue injury alone, it would appear, therefore, that neo-arsphenamin is somewhat more desirable for the treatment of syphilis than arsphenamin, but other factors are to be considered and the subject is ably discussed from the clinical standpoint by Dr. Schamberg.⁴ Neo-arsphenamin in a single massive dose (0.200 gm. per kilo) produced somewhat less marked histologic changes than single large doses of arsphenamin (0.100 gm. per kilo); likewise in smaller multiple doses neo-arsphenamin (0.02 to 0.03 gm. per kilo) produced similar but even less conspicuous tissue injuries than arsphenamin (0.01 gm. per kilo).

CONCLUSIONS

1. The intravenous injection of single massive and multiple smaller doses of neo-arsphenamin into rats and rabbits produces vascular

3. Kolmer, J. A., and Yagle, E. M.: Hemolytic Activity of Solutions of Arsphenamin and Neo-Arsphenamin, *J. A. M. A.* **74**:643 (March 6) 1920.

4. Schamberg, J. F.: Clinical Commentary on Studies of Histologic Changes in Organs Induced by Arsphenamin, by Neo-Arsphenamin and by Mercury, *Arch. Dermat. & Syph.*, this issue, p. 571.

injury, cellular degenerations and necrosis similar to those produced by solutions of disodium arsphenamin. The histologic changes found in the cerebrum, cerebellum, brain stem, meninges, heart, lungs, liver, kidneys, suprarenals and spleen are described. *

2. The tissue changes produced by neo-arsphenamin are less severe than those produced by solutions of disodium arsphenamin when considered in relation to dosage per kilo of body weight.

3. The changes described were produced in equal degree and with equal frequency by neo-arsphenamin prepared by different laboratories.

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A STUDY OF THE HISTOLOGIC CHANGES PRODUCED EXPERIMENTALLY IN RABBITS BY MERCURIAL COMPOUNDS *

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PHILADELPHIA

As shown in the preceding articles,¹ the administration of arsphenamin and neo-arsphenamin to rabbits by intravenous injection in multiple small doses comparable with those given to human beings according to body weight may result in the production of certain tissue changes in the internal organs. By reason of the practical importance of these changes in relation to the treatment of syphilis, Dr. Jay F. Schamberg suggested that we conduct a similar study of the mercurial compounds commonly administered in the treatment of syphilis, which would permit a comparison of the kind and extent of the histologic changes produced by these preparations with those produced by arsphenamin and neo-arsphenamin.

It is well known that preparations of mercury may exert injurious effects on the kidneys and that careful examinations of the urine are indicated during the treatment of syphilis with these preparations for evidences of renal irritation. In a previous study by one of us (Kolmer) of these lesions produced experimentally in rabbits,² well defined tubular and diffuse nephrites were commonly found, the severity of the lesions bearing some relation to the kind of compound administered, the percentage of mercury contained and the duration of life.

* From the Dermatological Research Laboratories of Philadelphia and the McManes Laboratory of Pathology of the University of Pennsylvania.

* Investigation aided by funds accruing from the preparation of arsphenamin.

1. Kolmer, J. A., and Lucke, B.: A Study of the Histologic Changes Produced Experimentally in Rabbits by Arsphenamin, *Arch. Dermat. & Syph.*, this issue, p. 483. *Ibid.*: A Study of the Histologic Changes Produced Experimentally in Rabbits by Neo-Arsphenamin, *Arch. Dermat. & Syph.*, this issue, p. 515.

2. Schamberg, J. F.; Kolmer, J. A., and Raiziss, G. W.: A Study of the Comparative Toxicity of the Various Preparations of Mercury, *Jour. Cutan. Dis.*, December, 1915.

A few reports are to be found in literature bearing on the nephritis produced by mercuric chlorid; an excellent study of experimentally produced nephritis has been made by Elbe.³ Burmeister and McNally⁴ and MacNider.⁵ These investigators have considered the kidney lesions dependent on the action of the mercury on the vascular tissues of the kidney, to the action of the metal as such on the parenchyma during elimination or to shock associated with severe mercury enteritis and the development of acid intoxication.

PURPOSES OF INVESTIGATION

Our purpose was to study the histologic changes produced in some of the internal organs of rabbits by different preparations of mercury administered by mouth and inunction and by intramuscular and intravenous injection, as commonly employed in the treatment of syphilis. In our studies bearing on the histologic changes produced in the rabbit by arsphenamin and neo-arsphenamin, massive doses were administered to intensify the pathologic changes, in addition to multiple small doses, but in this investigation only small doses of the mercurials were administered comparable with the maximum therapeutic doses commonly employed in the treatment of syphilis.

EXPERIMENTAL

Adult rabbits were employed in all experiments.

Necropsy examinations of the majority of animals were made at chosen intervals, and the following organs placed in 2 per cent. neutral liquor formaldehydi or in Orth's fluid for fixation followed by the preparation of paraffin sections stained with hematoxylin and eosin: cerebrum, cerebellum and brain stem, meninges, heart, lungs, spleen, liver, kidneys, and suprarenal glands. When animals died during the term of an experiment, necropsy examinations were performed within a few hours.

3. Elbe: Die Nieren und Darmveränderungen bei der sublimat Vergiftung des Kaninchens in ihrer Abhängigkeit vom gefassnerven System, Virchows Arch. f. path. Anat. **182**:445-498, 1905.

4. Burmeister, W. H., and McNally, W. D.: Acute Mercury Poisoning. A Parallel Histological and Chemical Study of the Renal and Hepatic Tissue Changes as Compared with the Rapidity of Absorption and the Amount of Mercury Present in the Circulating Blood at the Time Such Changes Occur, J. Med. Research **36**:87, 1917.

5. MacNider, W. deB.: A Study of Acute Mercuric Chlorid Intoxications in the Dog, with Special Reference to the Kidney Injury, J. Exper. Med. **27**: 519-538, 1918.

PART ONE: HISTOLOGIC CHANGES PRODUCED BY THE INTRA-
MUSCULAR INJECTION OF INSOLUBLE PREPARATIONS
OF MERCURY

Three rabbits received from six to twelve intramuscular injections of salicylate of mercury in sterile olive oil in dose of 0.002 gm. per kilogram of weight which is equivalent to 0.120 gm. or about 2 grains per 60 kilos or 130 pounds; the injections were made at intervals of one week in the muscles of the thighs.

Three rabbits received from four to six intramuscular injections of calomel in sterile olive oil in the same amounts and in the same manner as the salicylate of mercury.

Three rabbits received from eight to fourteen intramuscular injections of mercurial oil (gray oil) in the same amounts and in the same manner as the salicylate of mercury and calomel.

Table 1 shows the total number of injections given and the influence on the duration of life of each animal.

TABLE 1.—INTRAMUSCULAR INJECTION OF INSOLUBLE MERCURIAL PREPARATIONS IN A DOSE OF 0.002 GM. PER KILO ONCE A WEEK

Weight, Gm.	Compound	Amount of Pure Mercury per Kilo per Dose	Number of Injec- tions	Total Amount of Pure Mercury Adminis- tered per Kilo	Results
1,330	Salicylate.....	0.0012	6	0.0072	Living
1,420	Salicylate.....	0.0012	12	0.0144	Living
1,370	Salicylate.....	0.0012	9	0.0108	Died
1,500	Calomel.....	0.0017	4	0.0068	Died
2,300	Calomel.....	0.0017	6	0.0102	Died
1,500	Calomel.....	0.0017	9	0.0153	Died
3,500	Mercurial oil (gray oil).....	0.002	11	0.022	Living
1,680	Mercurial oil (gray oil).....	0.002	8	0.016	Died
1,800	Mercurial oil (gray oil).....	0.002	13	0.026	Living

I. HISTOLOGIC CHANGES PRODUCED BY THE INTRAMUSCULAR
INJECTIONS OF SALICYLATE OF MERCURY

Cerebrum, Cerebellum, Brain Stem and Meninges.—No conspicuous tissue changes were found. There were no notable vascular engorgement, no thromboses or focal hemorrhages. In one animal which had received nine injections, several small vessels were surrounded by jackets of small round cells, occasionally four to six layers in thickness. The ganglion cells generally presented a normal appearance.

Heart.—The pericardium and endocardium were normal. There was no increase of interstitial tissue in the myocardium. The blood vessels presented no changes, the heart muscle fibers stained well.

possessed clear nuclei and showed normal striations. No infiltrating cells were seen.

Lung.—The pleural surfaces were normal. All animals showed a slight engorgement of the alveolar capillaries, particularly one animal which died after nine injections. In this animal many of the air sacs were filled with edematous fluid. There were nowhere any areas of consolidation or fibrous tissue overgrowth. A few blood vessels contained smooth, hyaline material. Aside from slight congestion associated in one instance with moderate edema, no tissue changes were induced.

Spleen.—The capsule and trabeculae were normal. The follicles were of average size, well defined and occasionally showed prominent germinal centers. A moderate engorgement of the blood vessels was present. The pulp cords were of average width and contained the usual type of splenic cells. Hemosiderin pigment was nowhere present. The fibrillar reticulum appeared normal.

Liver.—The external capsule was normal. There was no increase of periportal connective tissue; the biliary ducts were normal. The blood channels were moderately filled with well preserved erythrocytes. The liver cells were well defined, stained well and possessed normal nuclei. No pigment deposits were present. One animal presented a curious condition; the liver cells were large, averaging about twice their normal size. Their outlines were unusually distinct. The cell protoplasm appeared absent or consolidated into coarse granules. The nuclei, however, were well preserved and showed no changes. It seemed as if the cells were distended and their protoplasm had become clumped together or had entirely disappeared. Since some normal control rabbits showed an identical condition, this change cannot be attributed to the medication and no further discussion of the condition is warranted.

Kidneys.—The renal capsules were unaltered. In none of the animals were there any noteworthy vascular changes, but all animals presented tubular degeneration, differing in degree according to the number of injections received. In the rabbits which received six injections the cells of the convoluted tubules were generally slightly swollen and somewhat granular. Occasional anuclear cells, often with many irregular small vacuoles, were found. Frequently the cell changes appeared to be irritative rather than degenerative. The glomeruli were moderately engorged and unaltered. In the animal which received nine injections the cells of the convoluted tubules and to a lesser degree of the thick portions of Henle's loops, possessed irregular outlines, were swollen or shrunken, frequently contained many minute vacuoles or coarse granules and were frequently anuclear. Often a more or less

granular precipitate or hyalin material filled or partly filled the tubular lumena. The glomeruli occupied about four fifths of the capsular spaces and their loops were well filled; endothelial proliferation was not apparent. The capsular spaces frequently held some granular or hyaline precipitate. One portion of the kidney showed a thin triangular streak of richly cellular connective tissue extending from the corticomedullary junction to the periphery. The tubules in this region had entirely disappeared; a few glomeruli could be still recognized as more or less fibrous nodules with greatly thickened capsular remnants. This



Fig. 1.—Rabbit; twelve intramuscular injections with salicylate of mercury. Kidney: Some tubules contain plugs of calcium salts; the epithelial lining of such tubules is necrotic and heavily infiltrated with lime granules. The section was taken from the outer cortex where calcification was most frequently encountered.

young scar tissue closely resembled a healed infarct. In the rabbit that received twelve injections distinct degenerative changes were apparent. The cells of the convoluted portions, particularly in the outer cortex, were swollen and granular, or vacuolated and shrunken. Many anuclear and frankly necrotic tubules were seen; these often contained plugs of calcium deposits (Figs. 1 and 2). In some of the disorganized cells fine granules of lime were encountered. While these changes were pro-

nounced in a few places, only relatively small areas of the kidney parenchyma were entirely destroyed; regeneration of cells was frequently seen.

The glomeruli generally filled about four fifths of the capsular spaces and presented no notable alteration excepting the presence of granular or hyaline precipitate in the capsular spaces (Fig. 3). Many of the thick portions of Henle's loops showed swollen, granular or vacuolated cells; the collecting tubules appeared normal.

Suprarenal.—Sections of the suprarenal glands did not show any constant or well defined changes from the normal.

II. HISTOLOGIC CHANGES PRODUCED BY THE INTRAMUSCULAR INJECTION OF CALOMEL

Cerebrum, Cerebellum, Brain Stem and Meninges.—As in the animals which received salicylate of mercury, conspicuous changes were not found in the central nervous system. Occasionally more or less marked perivascular lymphocytic infiltration was encountered; otherwise there were no vascular or cellular alterations.

Heart.—Only one rabbit, succumbing after nine injections, showed tissue changes. In several places there were rather small, poorly staining areas in the outer half of the right ventricular wall. The muscle cells here were poorly outlined and swollen and contained many fairly well circumscribed small vacuoles. The muscle nuclei in the affected fibers were frequently pale and pyknotic, and sometimes entirely absent.

Lungs.—Pleural changes were not produced. Only in the one animal that died after nine injections were definite morbid changes to be seen. Here the majority of the air spaces were filled with a smooth or occasionally finely granular material containing a moderate number of erythrocytes in various stages of lysis. Occasionally other cells were encountered in this apparently mechanical transudate. There were likewise no inflammatory cells within the lumina of the bronchial tubes, but many of these branches contained material similar to that in the air spaces. The alveolar capillaries were moderately congested. Changes were not present in the interstitial tissues.

Spleen.—In two animals large quantities of coarsely granular, golden brown pigment (hemosiderin) was found scattered throughout the pulp cords and the reticular framework. The pigment granules frequently occurred in the form of thick clumps, but occasionally fine dustlike material was seen engulfed by large endothelial phagocytes (Fig. 4). The blood channels were moderately dilated and contained many fragmented erythrocytes. "Shadow-cells" were quite prominent. No foreign cells were seen in noteworthy numbers, nor were there any

striking changes in the appearance of the splenic cellular elements. The walls of the venules appeared more prominent in the one animal that had received nine injections. The follicles in all the animals were of normal size or slightly increased and well outlined. Their germinal

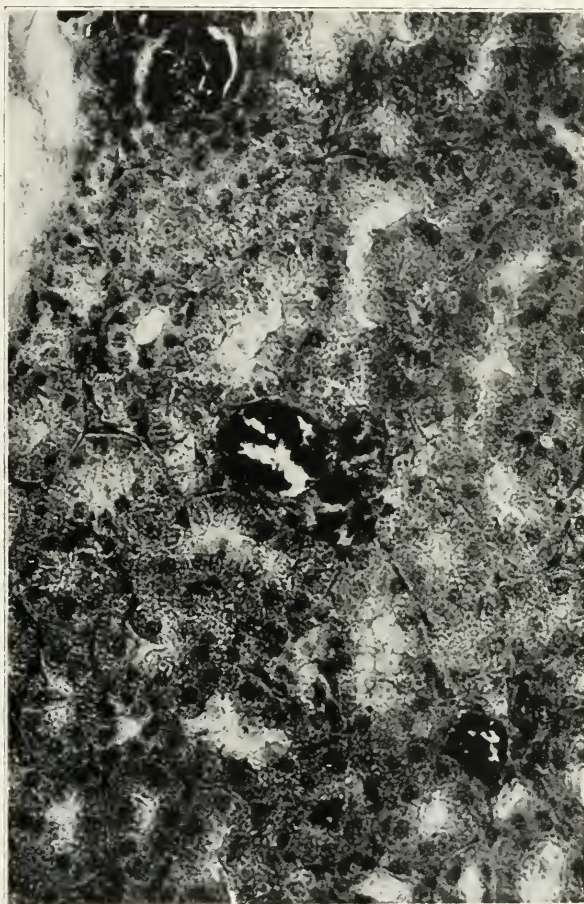


Fig. 2.—Rabbit; twelve intramuscular injections with salicylate of mercury. Kidney: This is a higher power photograph of the preceding illustration (Fig. 1). Three tubules containing plugs of calcium salts and calcified necrotic cells are shown. The lining cells of most of the other convoluted tubules are cloudy, swollen and frequently contain fine (fat) droplets. The nuclei often take a pale stain.

centers were occasionally very large. The arteries showed no structural alterations.

Liver.—The periportal connective tissue in one animal appeared slightly increased in quantity; the individual cells were larger than nor-

mal and possessed a fair amount of protoplasm with pale vesicular nuclei. This connective tissue proliferation, however, never assumed striking proportions. The sinusoids were moderately engorged and many fragmented erythrocytes were encountered. The cells generally were normal in size and staining quality, although in one animal there was some cloudy swelling. No conspicuous blood or bile pigment was to be found. The biliary ducts were normal.

Kidneys.—The kidneys of the two animals which succumbed after four and six injections presented only slight changes. There was no noteworthy increase of interstitial connective tissue, only a few glomeruli

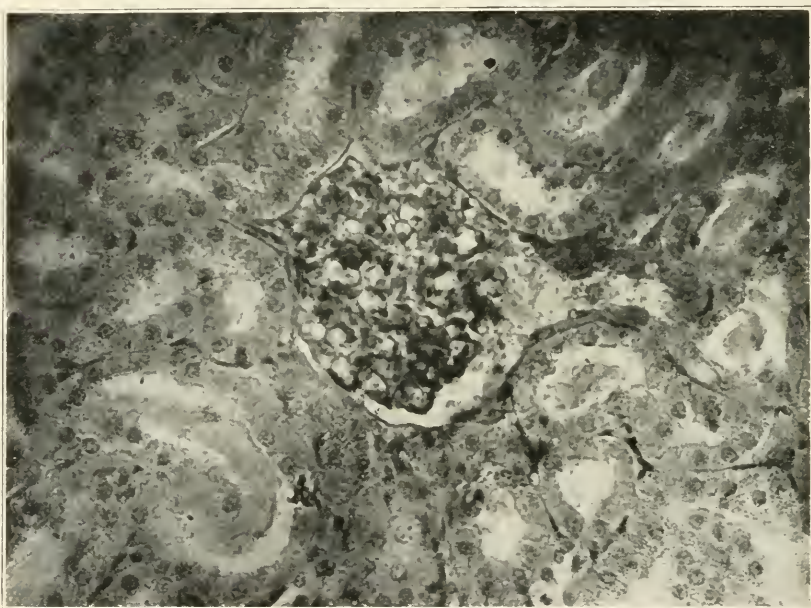


Fig. 3.—Rabbit; twelve intramuscular injections with salicylate of mercury. Kidney: The glomerular space contains granular, eosin-staining precipitate (albuminous fluid). Similar material is present within the lumina of many of the convoluted tubules. The renal cells are swollen and often possess a pale staining nucleus; absence of the nucleus is frequently encountered.

showing a little new formed pericapsular fibrous tissue. The larger vessels possessed normal walls. The glomerular capillaries were well filled; no increased cellularity was seen. Many convoluted tubules possessed swollen, granular and finely vacuolated cells; a moderate number presented nuclear degeneration.

In the animal which received nine injections the renal changes were marked and striking. There was a definite increase of interstitial tissue, the component elements being chiefly young and cellular. This

fibrosis was chiefly local and occurred in stitch-like triangular areas with the base of the triangle at the cortical periphery and the apex in the outer half of the medulla. The renal tubules in such regions were either collapsed and presented only narrow clefts or widely dilated cystlike structures (Fig. 5). In the latter case the tubular cells were of the normal flat and compressed type; many were partially degenerated. Where the fibrosis was less marked or not apparent, the convoluted tubules generally had more or less degenerated lining cells. The degree of retrogression varied from a mere cloudy swelling to protoplasmic vacuolation ("fatty degeneration") and frank necrosis.

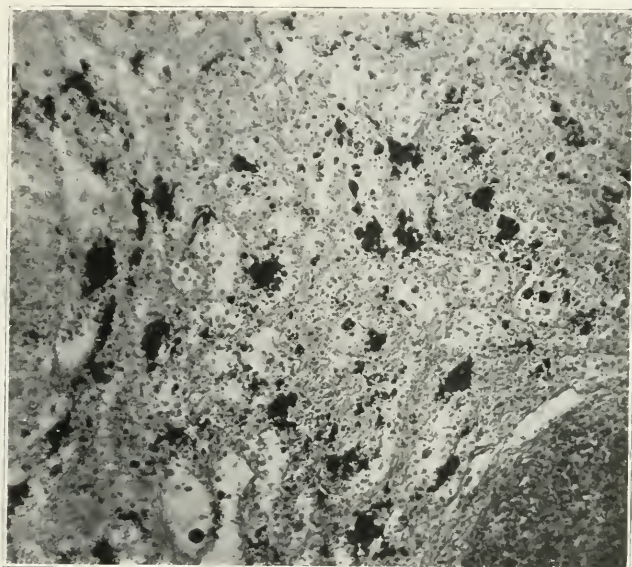


Fig. 4.—Rabbit; four intramuscular injections with calomel. Spleen: Considerable hemosiderosis is present (black in photograph). The hemosiderin granules occur as fine particles within phagocytic cells and as coarser granules free in the tissue. Some animals of other series presented a more marked pigmentation.

Casts of desquamated and necrotic cells were sometimes seen. In a number of tubules conglutinated masses of erythrocytes were present. Calcium granules were nowhere definitely seen, but a few cells took a deep basic stain indicating possible enrichment with lime salts. As a rule, the convoluted tubules were especially injured, but the straight tubules also had some swollen cells with indistinct outlines.

The capillaries were moderately engorged and often contained agglutinated erythrocytes. Many glomerular loops were collapsed and in some instances the entire tuft was shrunken. The capsular spaces

sometimes contained precipitated albuminous fluid and occasionally a few erythrocytes. No swelling of the capsular epithelium was noted. The capsules were nowhere definitely thickened but a slight pericapsular fibrosis was sometimes encountered.

III. HISTOLOGIC CHANGES PRODUCED BY THE INTRAMUSCULAR INJECTION OF MERCURIAL OIL (GRAY OIL)

Cerebrum, Cerebellum, Brain Stem and Meninges.—There were more pronounced alterations in this series than in the two preceding groups, possibly due to the fact that the animals received a greater number of injections. The arachnoid was more or less infiltrated with small round cells often grouped about blood vessels (Fig. 6). A slight



Fig. 5.—Rabbit; nine intramuscular injections with calomel. Kidney: A cortical area of fibrosis, cystic dilatation of tubules, tubular collapse and small round cell infiltration. Such areas are now and then encountered in the cortex. It must be remembered that "normal" rabbits are prone to develop renal sclerosis, and it is therefore sometimes difficult to decide whether such lesions are the result of the experiment. In a considerable number of control rabbits fibrotic areas in the kidney were encountered less frequently than among the experimental animals. In the experimental lesions there was usually a more or less marked small round cell infiltration, while this was little in evidence in the renal scars of control rabbits.

edema was present. Many of the vessels here, as well as in the brain, were distended with conglutinated masses of erythrocytes. In all animals many vessels were surrounded with a jacket of small round cells; sometimes this jacket consisted of only a single or double layer of

these cells but not infrequently a many-celled layer was encountered (Fig. 7). Occasionally minute areas of small round cell infiltration averaging about 0.1 to 0.2 mm. in diameter were found, but it was not always possible to decide whether or not these cell aggregations were perivascular as the centers of such groups frequently consisted of broken up masses and granular débris (Fig. 8). Intermingled with the small round cells were larger elements with a pale nucleus, possibly

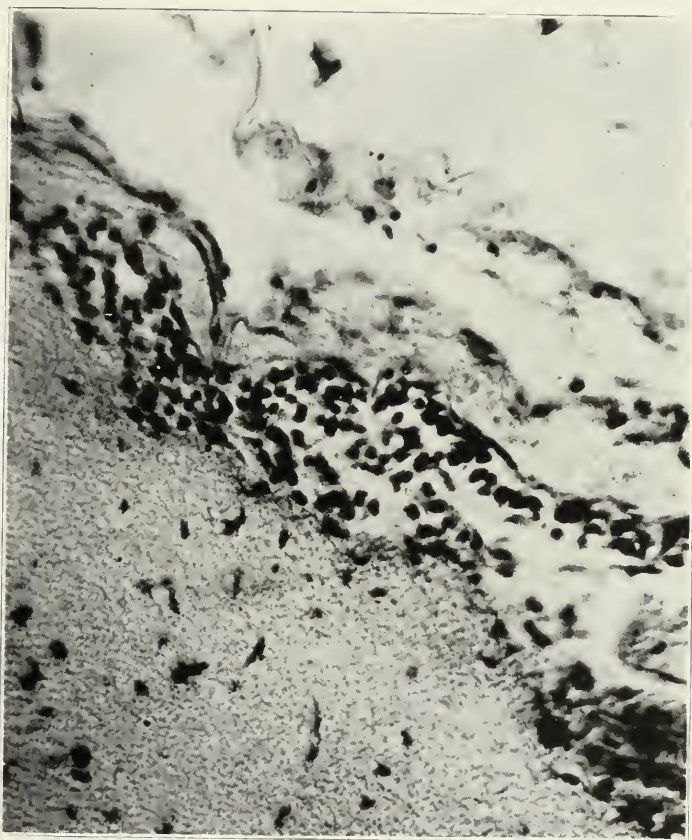


Fig. 6.—Rabbit; eleven intramuscular injections with mercurial oil (gray oil). Brain and Pia Arachnoid: Cellular infiltration and edema of the pia arachnoid. The cells are mainly of the small round cell (lymphocytic) type, but larger elements of the plasma cell type are here and there present.

endothelial derivatives; plasma cells were likewise present. The ganglion cells showed no distinct alterations excepting that here and there a few possessed excentric or pale nuclei.

On the whole, the changes described were most evident in the animal which had received thirteen injections.

Heart.—There was a well defined focal small round cell infiltration, the clefts between the muscle fibers being in places packed and distended with various sized round cells. The majority of these elements had small compact nuclei and but little cytoplasm, but intermingled were larger types with pale nuclei and more abundant cytoplasm. The latter resembled endothelial cells. A few corpuscles of the plasma cell type were likewise found. These cellular groups were scattered and did not occur in any particular region. Where the intermuscular clefts were

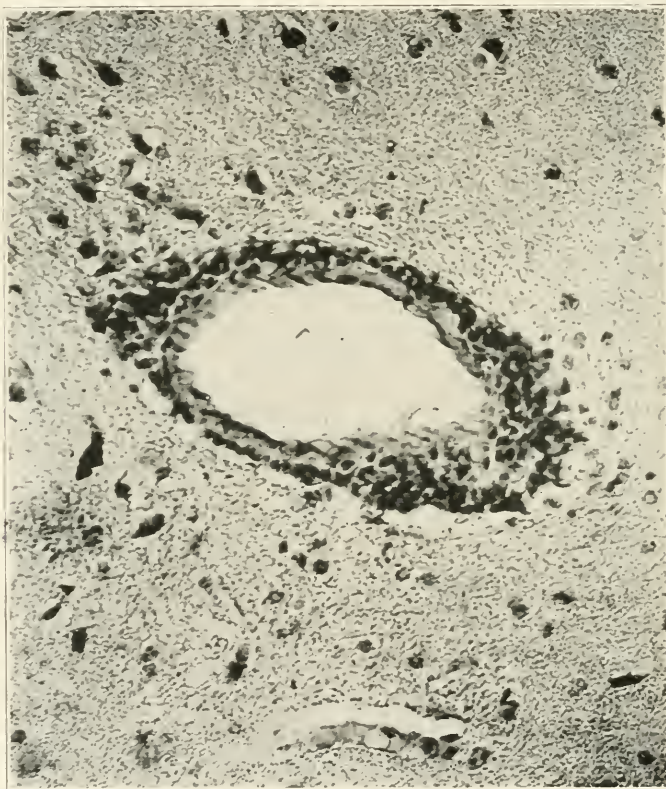


Fig. 7.—Rabbit; eight intramuscular injections with mercurial oil (gray oil). Brain: Perivascular round cell infiltration. The perivascular jacket consists of several layers of small and large round cells. Many of the vessels possessed such jackets.

densely packed, the intervening muscle cells appeared compressed and small and frequently degenerated (Figs. 9 and 10). Thus, we saw loss of transverse striations, small clear fat vacuoles, and other vacuoles containing a bit of reddish staining albuminous fluid. Outside of this focal cellular infiltration the heart muscle was generally well stained and apparently normal, but there were a few small vacuolated fibers.

The blood vessels often contained conglutinated erythrocytes and a slight swelling of the intimal endothelium was encountered. There appeared to be a proliferation of the perivascular fibrous tissue which sometimes contained some few small round cells (Fig. 11). This process was nowhere sufficiently definite to speak of a perivascular small round cell infiltration. The endocardial and epithelial tissues were rather loosely arranged and slightly edematous.

Lungs.—The alveolar capillaries were moderately engorged, and in one animal which died after four injections greatly dilated. In this animal much edematous fluid was present. A few hemosiderin-containing phagocytes were present in the air spaces. Local collapse was occasionally encountered. Agglutination and partial hemolysis of erythrocytes was present in many of the blood vessels. There were no conspicuous bronchial or pleural changes.

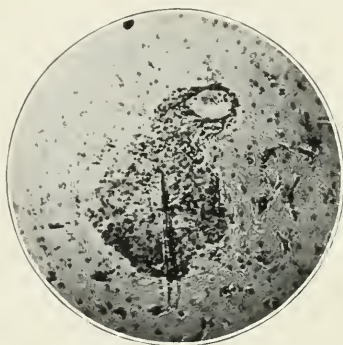


Fig. 8.—Rabbit; eleven intramuscular injections with mercurial oil (gray oil). Brain: A small area of perivascular infiltration extending considerably beyond the blood vessel; the latter is shown as a small dark ring. The cells are chiefly of the small round cell type.

Spleen.—The capsular and trabecular framework was unaltered. The blood channels were much dilated and frequently packed with agglutinated partly hemolyzed or degenerated erythrocytes. Large numbers of hemosiderin-phagocytes were present with coarser granules of hemosiderin in the pulp. The amount of hemosiderin varied in proportion to the number of injections received.

The follicles were large and distinct and their germinal centers were frequently prominent. The pulp cells were of the usual type; occasionally a megalokaryocyte was encountered; the arterioles were unaltered. Occasionally a slight swelling of the endothelial lung cells of the blood spaces was seen, but this change was nowhere conspicuous.

Liver.—In one animal which died after eight injections an extensive hemosiderin pigmentation of the liver cells was present. This pigmen-

tation was rather evenly distributed and was also well marked in the Kupfer-cells. Degenerated erythrocytes filled the sinusoids.

The livers of the other animals presented an inconspicuous hemosiderin pigmentation. The liver cells were generally normal, but increased granularity was observed in some sections. There were no alterations in the type and amount of connective tissue and of the bile ducts.

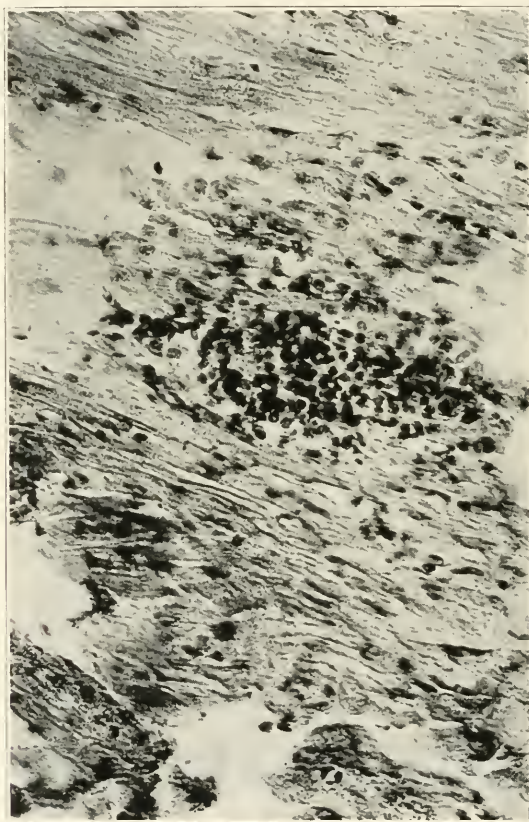


Fig. 9.—Rabbit; eight intramuscular injections with mercurial oil (gray oil). Heart: An area of round cell infiltration in the heart muscle. Such areas were frequently encountered among the animals of this series. The degree of infiltration varies from packing of the intermuscular clefts to actual necrosis of muscle fibers and dense accumulation of round cells in such degenerated areas. The photograph illustrates an intermediate degree; most of the cells are of the small round cell type, but a few larger elements are shown (see also Fig. 10).

Kidneys.—The changes corresponded roughly with the number of injections received. Here and there was a focal young connective tis-

sue increase which was particularly well marked around some glomeruli and between groups of cortical tubules (Fig. 12). Sometimes this proliferation had the form of a thin wedge, taking its origin at the periphery and narrowing to a point in the outer medulla. In such regions collapsed tubules and glomeruli were encountered. The vessels were generally moderately engorged, and often contained degenerated erythrocytes. The glomerular loops were in a similar condition. The



Fig. 10.—Rabbit; eight intramuscular injections with mercurial oil (gray oil). An area of round cell infiltration between the heart muscle fibers with destruction of a few fibers (see also Fig. 9).

glomerular coils filled about three fourths of the capsular spaces. A lightly eosin-staining precipitate was often present within the capsular spaces. The lining cells of the capsule were inconspicuously swollen. No thickening of the capsule was encountered, the proliferation mentioned being entirely perivascular.

The convoluted tubules and to a lesser extent the straight tubules possessed granular or frequently finely vacuolated (fat) cytoplasm.

Occasionally nuclear paling was seen. Their lumena contained lightly eosin-staining granular albuminous precipitates. Practically no desquamated cells were encountered. Nuclear multiplication was here and there present. Where vacuolization was well marked, cellular shrinkage resulted in a wider lumen.

The collecting tubules sometimes contained casts, but were otherwise unchanged; there were no calcium deposits.

Suprarenal.—The suprarenal glands showed no constant or conspicuous changes.

PART TWO: HISTOLOGIC CHANGES PRODUCED BY THE INTRAMUSCULAR INJECTION OF SOLUBLE PREPARATIONS OF MERCURY

Three rabbits received intramuscular injections of mercuric chlorid three times a week in a dose of 0.0004 gm. per kilogram of weight; this amount was equivalent to 0.024 gm., or about one third of a grain, per 60 kilos or 130 pounds.

Three rabbits received intramuscular injections of benzoate of mercury three times a week in a dose of 0.0005 gm. per kilogram of weight, which was equivalent to 0.03 gm., or one half of a grain per 60 kilos, or 130 pounds.

Table 2 shows the total number of injections given to each animal and the influence on the duration of life.

TABLE 2.—INTRAMUSCULAR INJECTION OF SOLUBLE PREPARATIONS OF MERCURY THREE TIMES A WEEK

Weight, Gm.	Compound	Dose per Kilo	Total Amount of Pure Mercury Adminis- tered per Kilo	Number of Injec- tions	Amount of Pure Mercury per Kilo per Dose	Results
3,200	Mercuric chlorid	0.0004	0.0018	6	0.0003	Living
2,350	Mercuric chlorid	0.0004	0.0054	18	0.0003	Living
1,720	Mercuric chlorid	0.0004	0.0036	12	0.0003	Died
1,330	Benzoate	0.0005	0.00108	6	0.00018	Living
3,240	Benzoate	0.0005	0.00216	12	0.00018	Living
2,580	Benzoate	0.0005	0.00324	18	0.00018	Living

I. HISTOLOGIC CHANGES PRODUCED BY THE INTRAMUSCULAR INJECTION OF MERCURIC CHLORID

Cerebrum, Cerebellum, Brain Stem and Meninges.—A distinct perivascular infiltration with small and large round cells was seen in many regions. This lymphocytic jacket consisted of one to several layers of cells. Many of the capillaries and smaller vessels were densely packed with small round cells, probably of the lymphocytic types (Fig. 13). A

slight perivascular edema was encountered. In one animal which received six injections a curious cell group was encountered consisting of a central area of necrosis about thirty microns in diameter (Fig. 14). About this area was a dense cluster of large cells (of the size of blood endotheliocytes) possessing a rather compact deep-staining eccentric nucleus, and finely or coarsely granular cloudy cytoplasm. These cells may be looked on as "granule-cells" (Körnchenzellen). This cell aggregation was in turn encircled by a triple and quadruple layer of small round cells (Fig. 15).

No distinct ganglionic cell changes were present. The pia arachnoid was mildly infiltrated with small round cells and its vessels surrounded with jackets similar to those in the brain tissue. Many of the smaller vessels in the brain were filled with agglutinated erythrocytes.

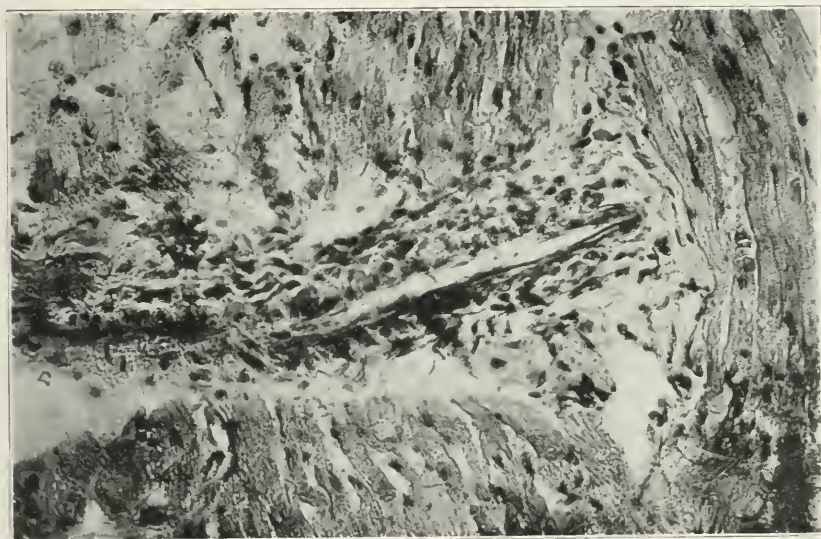


Fig. 11.—Rabbit: eight intramuscular injections with mercurial oil (gray oil). Heart: Round cell infiltration and early connective tissue proliferation about a small vessel in the heart muscle.

Heart.—No conspicuous alterations were present. There was a moderate capillary engorgement. The erythrocytes were often partly conglutinated; many capillaries contained a moderate excess of small round cells. On the whole, the muscle fibers stained well, but occasionally pale fibers with lost transverse striations and nuclear changes were encountered.

The interstitial connective tissue, the epicardium and the endocardium were normal.

Lungs.—A moderate congestion was found. Many capillaries and larger vessels contained conglutinated or partly hyalinized erythrocytes. One medium-sized vein contained a canalized thrombus, the new canal being lined by endothelium. A few new-formed capillaries were present within the blood mass (Fig. 16). Slight edema was found. Here and there the alveolar walls were thickened by round cell infiltration, elsewhere small areas of pulmonary collapse were encountered. The bronchi were normal. The pleural surfaces were normal.

Spleen.—These organs were engorged with much blood. An extensive hemosiderin pigmentation was present, the amount of the pigment roughly corresponding to the number of injections received.

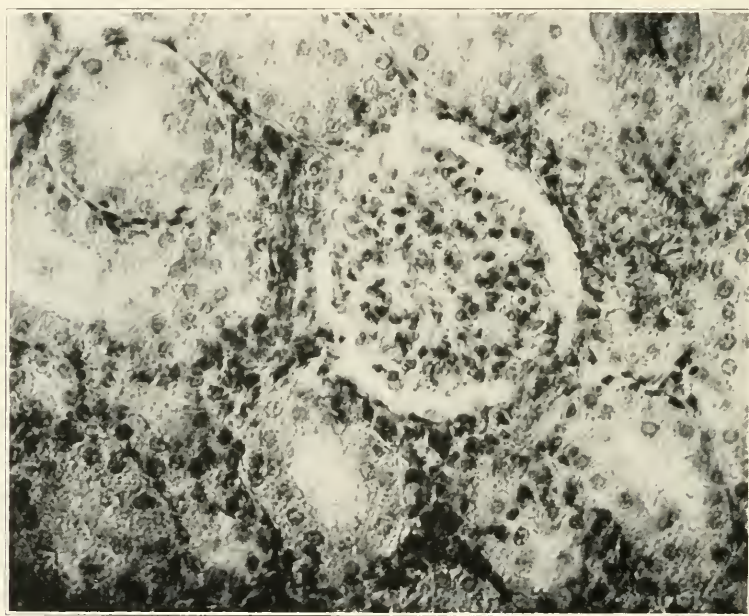


Fig. 12.—Rabbit; eight intramuscular injections with mercurial oil (gray oil). Kidney: A peritubular and periglomerular connective tissue proliferation and round cell infiltration is shown. Such lesions were focal rather than diffuse and occurred especially in the outer cortex.

Much of this pigment was within large phagocytic cells, but coarse granular masses were free in the tissue. The pulp cords appeared thinner because of the marked distention of the blood channels. The follicles were large, distinct and usually possessed well marked germinal centers. An occasional megalokaryocyte was seen in the blood channels. No distinct reticular or trabecular changes appeared to be present.

Liver.—There was a moderate engorgement, and many conglutinated erythrocytes were present. In the animal receiving the largest number

of injections the liver cells contained much finely granular hemosiderin. The periportal tissue was somewhat infiltrated, and in the animal which received eighteen injections, a slight connective tissue proliferation had taken place. The liver cells were not much altered; some granularity was found. The bile ducts were unchanged.

Kidneys.—The alterations were in direct proportion to the number of injections the animal received. A well-defined but not pronounced congestion was present in all animals. Much conglutination or solution of erythrocytes had taken place. The glomerular tufts almost or completely filled the capsular spaces; sometimes occluded or collapsed capillary loops were seen. In many capsular spaces there was gran-

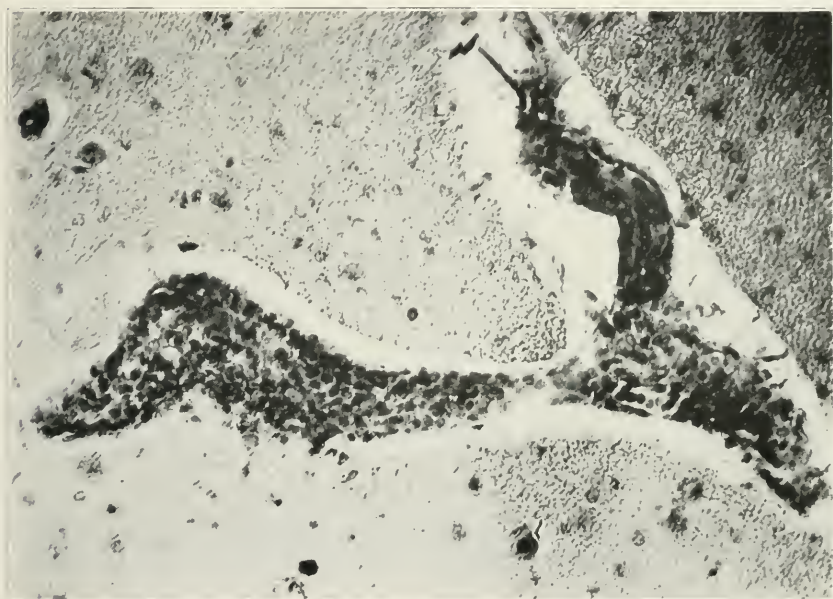


Fig. 13.—Rabbit; eighteen intramuscular injections with mercuric chlorid. Brain: The blood vessel shown is densely packed and completely surrounded with small round cells. The lesion is particularly striking because a longitudinal section of the blood vessel was obtained.

ular or homogeneous fluid, sometimes mingled with what appeared to be erythrocytic remnants. Similar material filled many of the tubular lumina, and in the animal which received eighteen injections such casts were particularly common, being often composed of more or less altered red blood cells (Fig. 18). The lining cells of the capsule were slightly swollen.

The convoluted tubules have chiefly suffered, Henle's tubules being less involved, while little or no change was present in the collecting

tubules. The mildest alteration amounted to swelling and greatly increased granularity with fine (fat) vacuolization as the next step; in some tubules the cellular outlines were lost with nuclear paling. Conspicuous necroses, however, were not found nor were calcium deposits encountered.

The interstitial changes were not well marked. There was slight edema, and in the advanced series some slight local fibrous proliferation about an occasional glomerulus. A few of Bowman's capsules were somewhat thickened.

Suprarenals.—The suprarenal glands showed no constant or definite histologic changes.

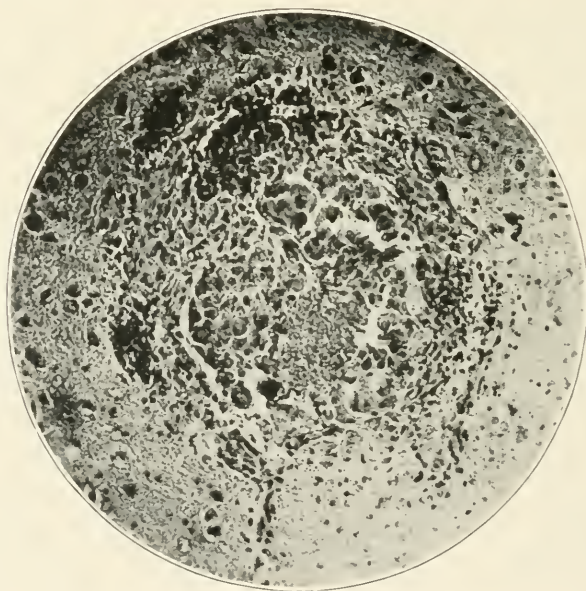


Fig. 14.—Rabbit; six intramuscular injections with mercuric chlorid. Brain: An area of necrosis, with many "granule-cells" and a wall of small round cells (see Fig. 15).

II. HISTOLOGIC CHANGES PRODUCED BY THE INTRAMUSCULAR INJECTION OF BENZOATE OF MERCURY

Cerebrum, Cerebellum, Brain Stem and Meninges.—The perivascular small round cell infiltration described in previous groups was well marked in this series (Fig. 19). In addition, many vessels were packed with lymphocytes with occasional small foci of round cell infiltration. Sometimes it was not possible in these cell groups to decide whether they constituted marked perivascular jackets or independent infiltration.

The pia arachnoid was well infiltrated with small round cells, particularly in the fissures. Small cortical vessels apparently coming from or going to the meninges possessed pronounced lymphocytic jackets.

The perivascular lymph spaces were dilated beyond the cellular infiltrations. Many blood vessels were engorged with conglutinated erythrocytes. A slight to moderate hyperemia was present, but hemorrhages were not encountered. No notable changes of the brain cells were seen.

Heart.—Conspicuous alterations were not present; occasionally the intermuscular spaces contained small groups of round cells. The heart

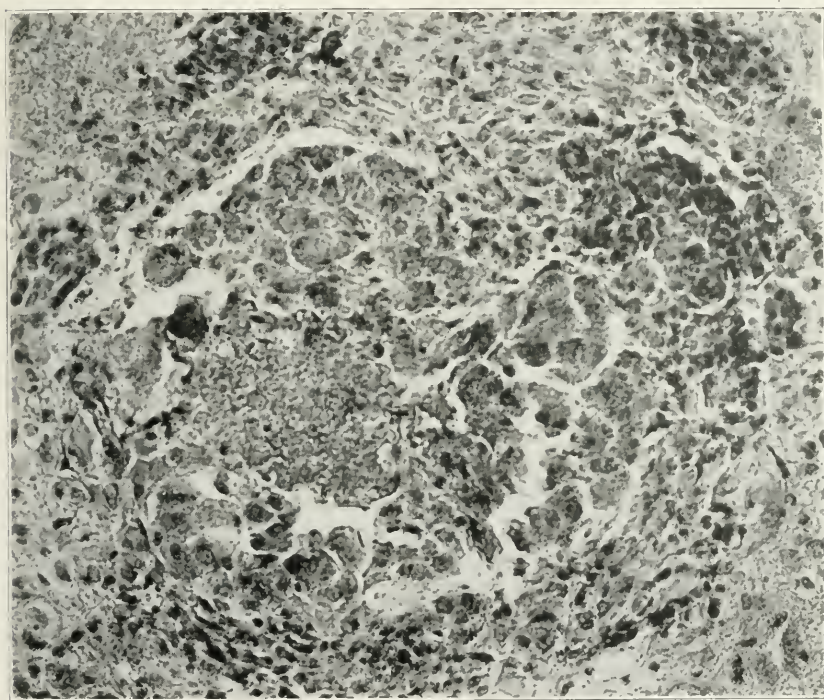


Fig. 15.—Rabbit; six intramuscular injections with mercuric chlorid. This is a high power photograph of the preceding section to bring out the necrotic area and the large "granule-cells."

fibers were occasionally swollen and possessed indistinct cross striations. The blood vessels showed no definite changes. The epicardium and endocardium were normal.

Lungs.—Many minute areas of collapse were seen, particularly near the pleural surfaces. These areas were usually hyperemic and edematous, and in some parts the edematous fluid filled the air spaces. Polymorphonuclear cells were not encountered. Small areas of compensa-

tory distention bordered on the atelectatic portions. The blood vessels frequently contained conglutinated or partly hyalinized masses of erythrocytes. The bronchioles appeared normal. The collapsed areas previously mentioned may have been caused by subfunction of the respiratory muscles.

Spleen.—Large quantities of coarsely granular golden brown pigment were scattered throughout the sections (Fig. 20). This pigment was partly engulfed in large phagocytic cells and partly free in the tissues. The blood channels were widely dilated and frequently con-

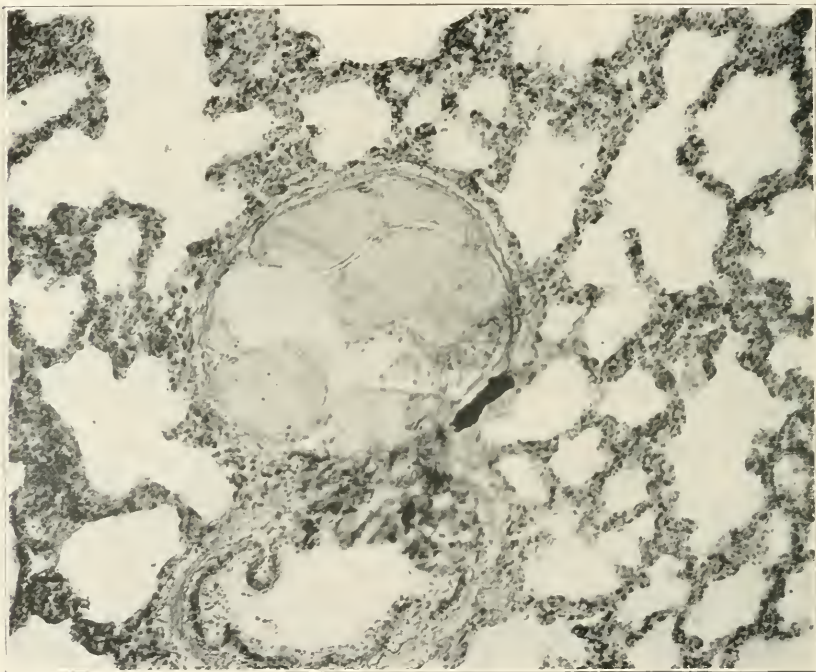


Fig. 16.—Rabbit; twelve intramuscular injections with mercuric chlorid. Lung: A medium-sized vein contains a canalized thrombus, the new canal being lined by endothelium; a few newly formed capillaries are present within the mass of blood.

tained more or less degenerated erythrocytes. Alteration of the vessel walls was not present. The trabeculae were normal; the pulp cords were somewhat compressed by the engorged sinusoids and venules. The follicles were large, well defined and sometimes contained rather large germinal centers.

Liver.—An inconspicuous increased cellularity about the portal canals was present, chiefly due to small round cells. Many liver cells were lightly dusted with hemosiderin; the Kupfer cells were frequently

pigmented. A moderate congestion was seen accompanied by an agglutination of erythrocytes. The liver cells presented no noteworthy changes.

Kidneys.—The changes vary in proportion to the number of injections received. Only unimportant alterations were present in the rabbits having received the minimum number of injections. In the other animals occasional long triangular areas of young connective tissue proliferation were encountered; in these regions the tubules were either small and collapsed or large and widely dilated with flattened epithelium.

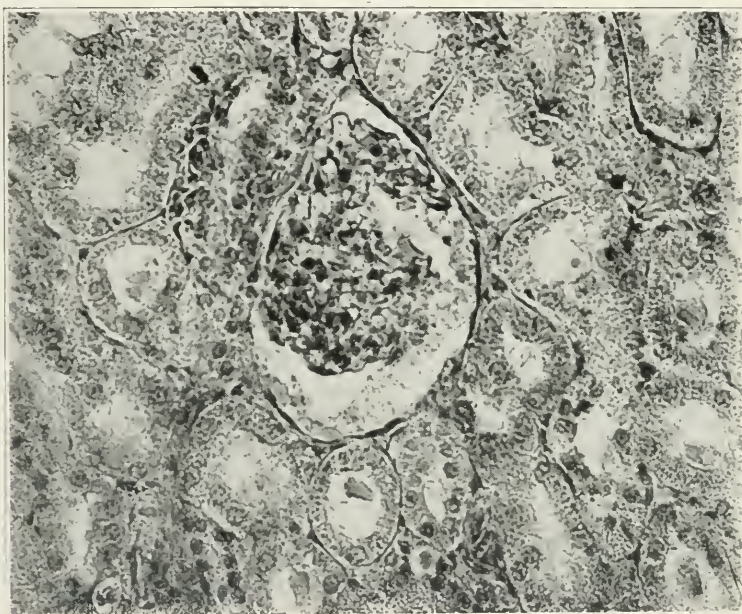


Fig. 17.—Rabbit; eight intramuscular injections with mercuric chlorid. Kidney: The capsular space and the lumina of several of the collecting tubules contain granular, eosin-staining material. The lining cells of the capsule are slightly swollen; the epithelium of the convoluted tubules is cloudy, swollen, often vacuolated and frequently anuclear.

The glomeruli were generally small and partly collapsed. Proliferating connective tissue occasionally occurred about the glomerular capsule and between tubules.

The convoluted portions of the tubules were chiefly affected. The changes here ranged from simple cloudy swelling to fatty vacuolization and ultimate shrinkage of the lining cells. Cellular desquamation was frequently encountered with degenerated epithelial cells partly filling the tubular lumina. Such cell casts were particularly conspicuous within the large collecting tubules in the medulla (Fig. 21). Some

hyaline casts were likewise seen and, infrequently, a few erythrocytes were found in the tubular lumina. There were many regenerating lining cells.

The vessels were moderately engorged and often contained conglutinated or partly hyalinized erythrocytes. A moderate degree of edema was present; this was especially well seen in the medullary portions.

Suprarenals.—The suprarenal glands showed no constant or conspicuous changes.

PART THREE: HISTOLOGIC CHANGES PRODUCED BY THE INTRAVENOUS INJECTION OF SOLUBLE PREP- ARATIONS OF MERCURY

Three rabbits were given intravenous injections of mercuric chlorid every five days in a dose of 0.0002 gm. per kilogram of weight, which was equivalent to 0.012 gm., or one fifth of a grain, per 60 kilos or 130 pounds.

Three rabbits were given cyanid of mercury in the same dose and in the same manner.

Three rabbits were given mercurophen in the same dose and in the same manner.

Table 3 shows the number of injections given each animal and the duration of life.

TABLE 3.—INTRAVENOUS INJECTION OF MERCURIAL COMPOUNDS IN A DOSE OF 0.0002 GM. PER KILO EVERY FIVE DAYS

Weight, Gm.	Compound	Amount of Pure Mercury per Kilo per Dose	Number of Injec- tions	Total Amount of Pure Mercury Adminis- tered per Kilo	Results
1,900	Mercuric chlorid.....	0.000148	6	0.000888	Living
2,320	Mercuric chlorid.....	0.000148	12	0.001776	Living
1,930	Mercuric chlorid.....	0.000148	14	0.002072	Living
2,060	Mercuric cyanid.....	0.000166	6	0.000996	Living
1,470	Mercuric cyanid.....	0.000166	12	0.001892	Living
3,040	Mercuric cyanid.....	0.000166	13	0.002058	Living
1,730	Mercurophen.....	0.000104	6	0.000624	Living
1,820	Mercurophen.....	0.000104	12	0.001248	Living
2,300	Mercurophen.....	0.000104	13	0.001352	Living

I. HISTOLOGIC CHANGES PRODUCED BY THE INTRAVENOUS INJECTION OF MERCURIC CHLORID

Cerebrum, Cerebellum, Brain Stem and Meninges.—Conspicuous lesions were not found. The pia arachnoid was mildly congested and an occasional small or large round cell was found. The brain vessels were slightly filled; definite perivascular cell infiltration was not found.

Some vessels contained clotted erythrocytes. The vascular endothelium was occasionally somewhat swollen. No areas of necrosis or groups of foreign cells were found. The ganglion cells presented no definite alterations.

Heart.—Occasional fibers took a pale stain, were somewhat granular, contained small clear (fat) vacuoles and were sometimes without nuclei. There was no congestion and no alteration of vessel walls, but some arterioles contained agglutinated erythrocytes. The interstitial connective tissue and the epicardium and endocardium were normal.

Lungs.—Conspicuous changes were not present. There was a slight congestion and an occasional air sac was filled with edematous material. The blood vessels sometimes contained agglutinated or hyalinized

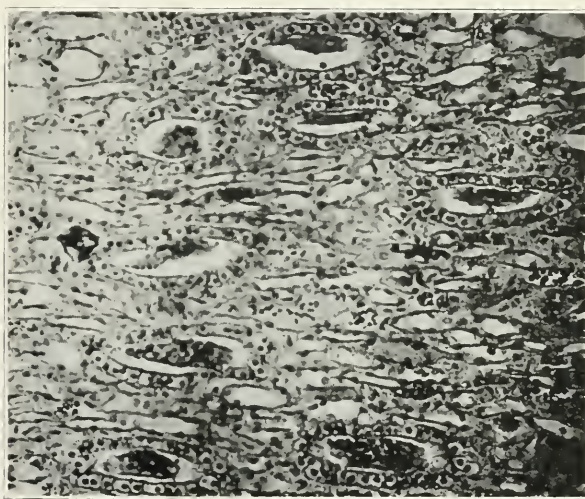


Fig. 18.—Rabbit; eighteen intramuscular injections with mercuric chlorid. Kidney: Casts composed of altered erythrocytes, granular debris and degenerated epithelium are present within many of the renal tubules. They are particularly well seen in the collecting medullary tubules. The interstitial tissue is somewhat edematous.

erythrocytes. The alveolar walls, bronchi and pleural surfaces were normal.

Spleen.—The blood channels were widely distended and contained moderate numbers of broken-down erythrocytes. A small number of hemosiderin phagocytes were present; only a little free hemosiderin was found. The pulp cords possessed the usual type of cells and seemingly an increased number of small round cells. The follicles were large with prominent germinal centers. Changes were not encountered in the vascular walls. The capsule and trabeculae were normal.

Liver.—A slightly increased granularity, slight hemosiderin pigmentation and a moderate congestion constituted the inconspicuous alterations. The periportal connective tissue was normal. Some agglutination and lysis of erythrocytes were seen.

Kidneys.—Occasionally a tubule with necrotic and calcified cells was encountered. These were mainly seen in the outer cortex and required careful search. Most convoluted tubules possessed slightly swollen, granular and open vacuolated (fat) cells; generally the nuclei stained and appeared normal. Sometimes homogeneous or coarsely granular eosin-staining casts were present, which were best seen in the collecting tubules. The glomeruli were of average size; there was no notable engorgement. Connective tissue proliferation was not found.

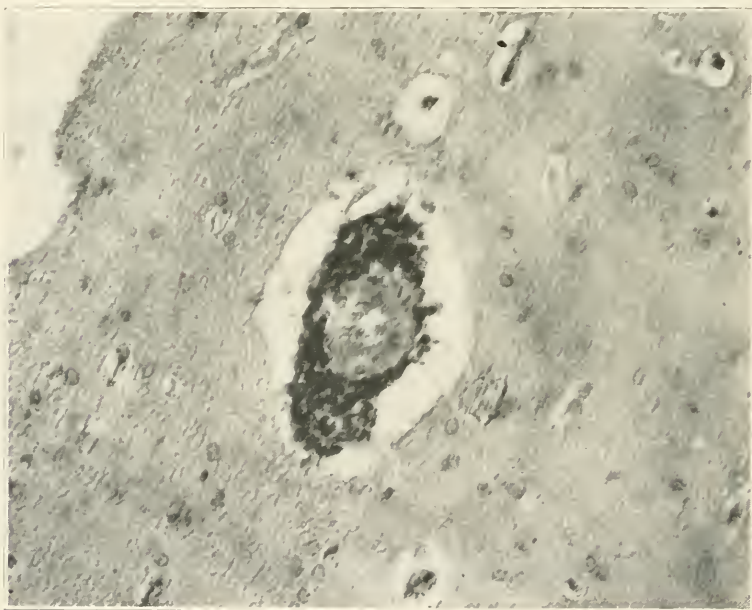


Fig. 19.—Rabbit; eighteen intramuscular injections with benzoate of mercury. Brain: Perivascular small round cell infiltration. The animals of this series, as well as of the preceding group, showed such lesions particularly well.

II. HISTOLOGIC CHANGES PRODUCED BY INTRAVENOUS INJECTION OF CYANID OF MERCURY

Cerebrum, Cerebellum, Brain Stem and Meninges.—The pia arachnoid was mildly infiltrated with small round cells. There were, however, larger cells with an eccentric reticular nucleus and pink staining cytoplasm. The vessels here as well as in the brain tissue were moderately engorged, and often contained agglutinated erythrocytes or hya-

line material. No definite perivascular jackets were present, but in some instances the vessels contained round cells of the types already mentioned. The vascular endothelium was somewhat swollen. Decided changes were not present in the ganglion cells.

Heart.—There were no conspicuous changes. Occasionally small groups of round cells occurred between slightly separated muscle fibers. On the whole the muscle fibers stained well and were normally nuclear; occasionally swollen fibers with lost striations and minute clear (fat) vacuoles were encountered. The capillaries were normally filled; con-

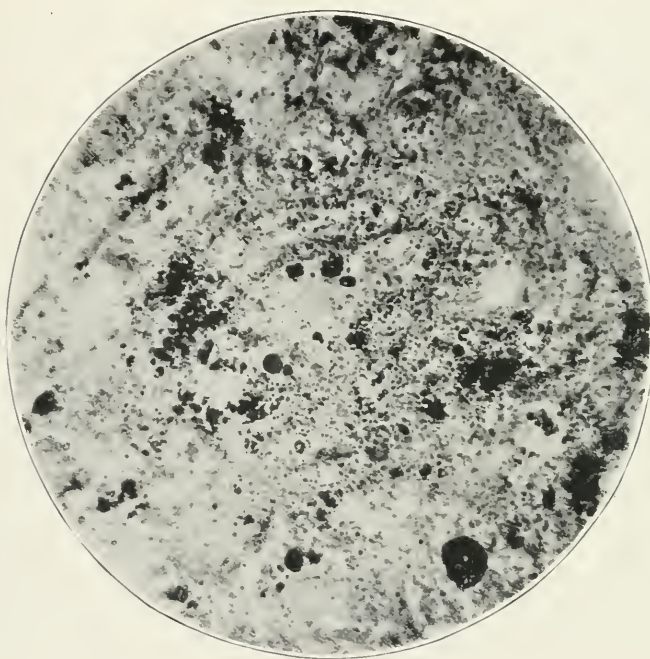


Fig. 20.—Rabbit; twelve intramuscular injections with benzoate of mercury. Spleen: Considerable hemosiderin pigment is scattered throughout the sections. The pigment occurs as fine dust within phagocytic cells and in the form of larger, not engulfed, particles.

glutination of erythrocytes was seen in a few places. The interstitial tissue and the epicardium and endocardium were normal.

Lungs.—These tissues were practically normal. Some vessels contained conglutinated or hyalinized erythrocytes which in a few appeared to have led to actual occlusions. The alveolar capillaries were mildly engorged. Some small areas were slightly edematous and partly collapsed; bronchial changes were not seen. There were no inflammatory cells. The pleural coverings were normal.

Spleen.—In proportion to the number of injections a mild hemosiderin pigmentation was encountered. The blood channels were well dilated and often packed with broken-down erythrocytes. The lining endothelial cells were slightly swollen. The follicles were large and distinct and possessed conspicuous germinal centers. There were no changes in the capsule or trabeculae.

Liver.—The periportal tissue was slightly cellular. The liver cells were a little more granular than usual and often contained dust-like hemosiderin and small clear (fat) vacuoles. There was a mild

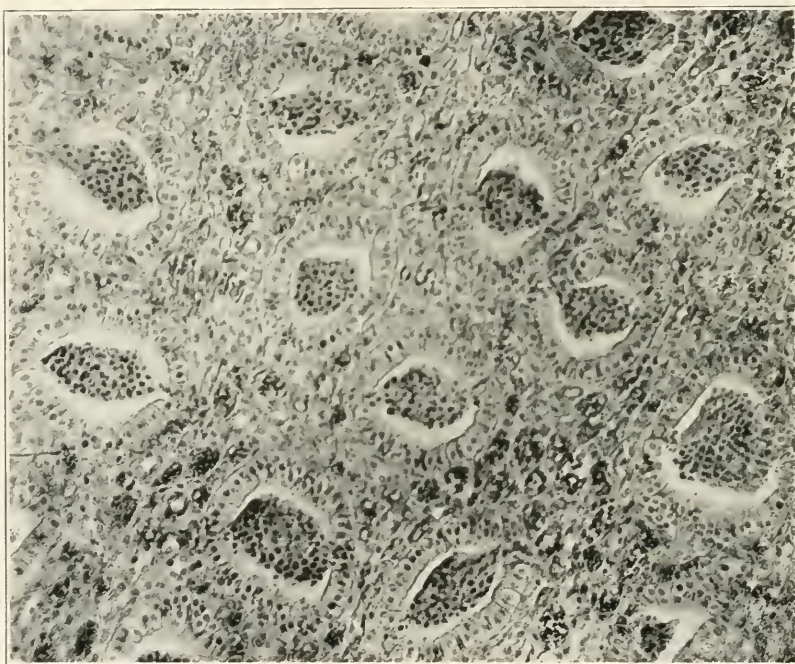


Fig. 21.—Rabbit; twelve intramuscular injections with benzoate of mercury. Kidney: Casts composed of desquamated and degenerated renal epithelium are present in the collecting tubules; the casts are derived from the lining of the convoluted tubules. A moderate interstitial edema is shown.

engorgement and there were a considerable number of conglomerated red cells. The Kupfer cells appeared somewhat more prominent and were frequently slightly pigmented.

Kidneys.—The changes varied in proportion to the number of injections and manifested themselves mainly in the convoluted tubules. The lining cells of these tubules were at first swollen and more granular; later fat droplets appeared, and finally a slight shrinkage of the cells with consequent widening of the lumina. Frank necroses were not

seen nor were the above alterations at all conspicuous. The limbs of Henle often possessed a ragged and apparently necrotic lining. Cellular and hyaline casts were seen occasionally, being particularly noticeable in the large collecting tubules which themselves possessed normal epithelial lining. The capillaries were moderately engorged and various vessels contained occasional clumps of conglomerated erythrocytes. The glomerular tufts were quite large and appeared normal. The capsular spaces frequently contained a little smooth or granular eosin-staining substance. The lining of Bowman's capsules was mildly swollen. Conspicuous connective tissue proliferation was not seen, but occasionally there were a few small triangular cortical areas of cellular fibrosis.

Suprarenals.—The suprarenal glands showed no conspicuous changes.

III. HISTOLOGIC CHANGES PRODUCED BY THE INTRAVENOUS INJECTION OF MERCUROPIHEN

Cerebrum, Cerebellum, Brain Stem and Meninges.—Occasionally a thin single or double layered jacket of small round cells was found around some of the blood vessels, particularly in the animal which received the greatest number of injections. Slight swelling of the vascular endothelium and some agglutinations or hyalinization of erythrocytes were also seen. The pia arachnoid contained a few infiltrating round cells. All of these changes were inconspicuous. Definite alterations of ganglion cells were not encountered.

Heart.—Notable lesions were not found. There was a mild congestion, and agglutination and hyalinization of erythrocytes were sometimes found. Occasionally muscle-fibers were devoid of well-defined striations and contained small (fat) vacuoles. The interstitial tissue and the epicardium and endocardium appeared normal.

Lungs.—All animals showed a moderate degree of congestion of the lungs associated with a mild degree of local rather than general edema. The bronchi and the pleural coverings were unchanged.

Spleen.—The blood spaces were moderately dilated and frequently packed with degenerating erythrocytes. A mild hemosiderin pigmentation was present. The vascular endothelium appeared slightly swollen. The trabeculae were normal. The follicles were large, well defined and possessed fairly prominent germinal centers. These changes varied in proportion to the number of injections.

Liver.—The hepatic cells, particularly those in the animals which received twelve or more injections, were swollen, often pigmented and contained many minute (fat) vacuoles. The cells were likewise

somewhat swollen and frequently pigmented. In the animal which received the greatest number of injections the periportal tissue was more cellular and contained a small number of round cells. The blood changes were as elsewhere in this group.

Kidneys.—The alterations were slight and varied in degree with the number of injections received. There was a mild congestion, the glomeruli were fairly large and a few possessed collapsed capillary loops. Conglutination and partial hyalinization of erythrocytes

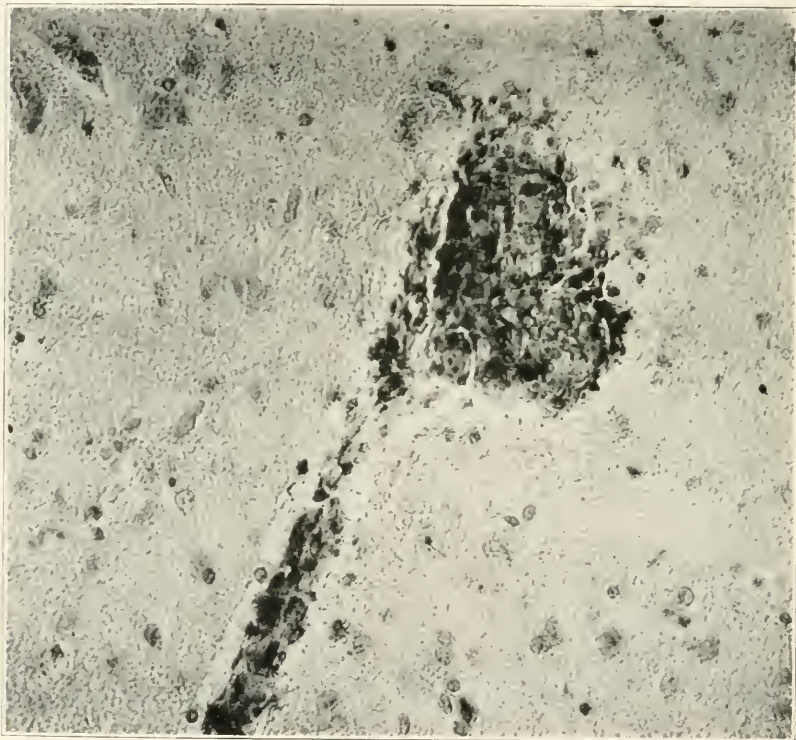


Fig. 22.—Rabbit; thirty-five doses by mouth of yellow mercurous iodid. Brain: Perivascular small round cell infiltration.

occurred in a moderate degree. Occasionally a few erythrocytes were found in the capsular spaces or within the tubular lumina. A slight amount of granular albuminous precipitate was likewise seen in these locations. The capsules and their linings appeared unaltered. The convoluted tubules were mainly involved. Here the cell changes ranged from a swelling to increased granularity, vacuolization, occasional nuclear disappearance and slight shrinkage of the cell. Not all convoluted tubules were equally affected; those in the outer cortex

presented the most definite involvement. No frank necroses were found. The straight and collecting tubules showed no, or the most inconspicuous, changes. There was nowhere definite edema or connective tissue increase.

Suprarenals.—The suprarenal glands did not show any constant or conspicuous changes.

PART FOUR: HISTOLOGIC CHANGES PRODUCED BY THE ORAL ADMINISTRATION OF YELLOW MERCUROUS IODID

Each of three rabbits were given daily a pill containing yellow mercurous iodid in a dose of 0.002 gm. per kilogram of body weight, which corresponded to 0.120 gm., or two grains per 60 kilograms, or about 130 pounds.

The first animal received twenty-four doses followed by necropsy; the second received twelve doses and the third thirty-five doses when necropsies were made. None of the animals died during the experiment, but necropsy examinations were made at these chosen intervals.

Table 4 shows the total amount of mercury administered in this manner.

TABLE 4.—THE DAILY ADMINISTRATION OF YELLOW MERCUROUS IODID BY MOUTH IN A DOSE OF 0.002 GM. PER KILO

Weight, Gm.	Amount of Pure Mercury per Kilo per Dose	Number of Doses	Total Amount of Pure Mercury Administered per Kilo	Results
2,575	0.0012	24	0.0288	Living
2,850	0.0012	12	0.0144	Living
2,600	0.0012	35	0.042	Living

Cerebrum, Cerebellum, Brain Stem and Meninges.—In the animal which received twelve doses discernible histologic changes were not encountered. In those animals which received twenty-four and thirty-five doses, more or less marked perivascular small round cell infiltrations were found (Fig. 22). These perivascular jackets consisted of from one to three or four layers of cells. The vascular endothelium was slightly swollen and a few vessels contained more or less conglomerated or partly hyalinized erythrocytes. An inconspicuous round cell infiltration was sometimes observed in the pia arachnoid. The brain cells appeared unchanged.

Heart.—In a few areas there were accumulations of round cells in the intermuscular tissue spaces. These cells were generally of the small round cell type, but some possessed larger and paler nuclei and more abundant protoplasm. The muscle cells in such regions were somewhat shrunken, stained more palely and showed a pyknotic

nucleus. On the whole, there were no important muscle changes, but occasional cells were swollen, devoid of definite cross striations and contained small (fat) vacuoles. The vessels were moderately filled, sometimes with conglutinated erythrocytes. The epicardium and endocardium were normal.

Lungs.—Depending on the amount of medication, there was more or less congestion with a mild accompanying edema. The alveolar walls appeared slightly thickened in the animal receiving thirty-six doses. The bronchial branches and the pleural surfaces were normal.

Spleen.—In the animal which received twelve doses, only a mild congestion was present; this was much more pronounced in the animals receiving twenty-four and thirty-five doses. In these the blood spaces



Fig. 23.—Rabbit; thirty-five doses by mouth of yellow mercurous iodid. Liver: An area of periportal connective tissue proliferation, small round cell infiltration. The biliary ducts are considerably increased in numbers.

were considerably dilated and often packed with degenerating erythrocytes and phagocytes containing hemosiderin. Hemosiderin also occurred free in the tissue in the form of coarse clumps. A mild swelling of the vascular endothelium was seen. A mild fibrillar fibrosis appeared in the animals having received thirty-six doses. The follicles were large, and frequently had prominent germinal centers. The pulp cords were compressed in proportion to the engorgement. The capsule and trabeculae were normal.

Liver.—There was a definite although mild change in the periportal tissue. The animals receiving fewest injections had a moderate degree

of infiltration of the portal tissues with small round cells and slightly elongated fibroblastic elements; the biliary ducts were normal. In the animal which received thirty-five doses there was a definite increase of periportal young connective tissue, intermingled with small round cells. Sometimes the connective tissue was becoming of adult type, but on the whole it was richly cellular. Usually this proliferation was confined to the neighborhood of the portal canals and bile ducts, but in several instances we saw a slight intralobular invasion. The biliary ducts were considerably increased in number and appeared to be actively proliferating in the fibrous overgrowth. The picture was much the same as in early human periportal fibrosis with bile duct proliferation. The hepatic cells were usually more granular and contained a



Fig. 24.—Rabbit; thirty-five doses by mouth of yellow mercurous iodid. Kidney: A focal peritubular connective tissue proliferation. Such foci were encountered only here and there and generally only in the cortex.

moderate quantity of fine dustlike hemosiderin. The Kupfer cells were usually slightly enlarged and frequently contained brownish or brownish-black granules. There was a slight engorgement, and the erythrocytes were often slightly conglomerated or partly hyalinized.

Kidneys.—The changes depended on the length of medication. In the animals receiving the shortest treatment the convoluted tubules frequently contained granular debris; their lining cells were swollen, more granular and sometimes finely vacuolated. The glomeruli were generally fairly large and had well filled loops. Changes in the capsules were not found. The collecting tubules were generally not

involved. These alterations were more pronounced in animals having received the maximum treatment. The convoluted tubules frequently showed vacuolated epithelium, and cellular shrinkage was sometimes quite plain. The limbs of Henle were likewise affected but the large collecting tubules appeared unchanged. The latter frequently contained, however, hyaline and granular casts. The glomeruli did not differ in any notable degree from the picture given above. There was a mild and rather inconspicuous connective tissue proliferation, chiefly about an occasional glomerulus or between cortical tubules. The erythrocytes presented the same changes as elsewhere.

Suprarenals.—The suprarenal glands showed no changes.

PART FIVE: HISTOLOGIC CHANGES PRODUCED BY THE ADMINISTRATION OF MERCURY BY INUNCTION

Each of three rabbits were rubbed daily for ten minutes with the official 50 per cent. mercurial ointment (gray ointment) in dose of 0.09 gm. per kilogram of body weight, corresponding to 5.4 gm., or about one and a half drams, per 60 kilos or 130 pounds. The hair had been previously removed with barium sulphid from several areas over the back and abdomen of each animal to facilitate thorough inunction.

Three additional rabbits received similar inunctions with a 50 per cent. ointment of calomel in the same manner.

Table 5 shows the total number of inunctions given each rabbit and the duration of life.

TABLE 5.—DAILY INUNCTIONS OF MERCURIAL PREPARATIONS IN A
DOSE OF 0.09 GM. PER KILO

Weight, Gm.	Compound	Amount of Pure Mercury per Kilo per Dose	Number of Injec- tions	Total Amount of Pure Mercury Adminis- tered per Kilo	Results
1,950	Mercurial ointment (gray ointment).....	0.045	7	0.315	Died
3,025	Mercurial ointment (gray ointment).....	0.045	18	0.810	Died
2,150	Mercurial ointment (gray ointment).....	0.045	17	0.765	Died
2,020	Calomel ointment.....	0.038	23	0.874	Died
3,350	Calomel ointment.....	0.038	7	0.266	Died
2,005	Calomel ointment.....	0.038	9	0.342	Died

I. HISTOLOGIC CHANGES PRODUCED BY THE INUNCTION OF MERCURIAL OINTMENT (GRAY OINTMENT).

Cerebrum, Cerebellum, Brain Stem and Meninges.—Many of the small vessels were surrounded with single or multiple layers of small round cells. This perivascular infiltration did not occur in the first

animal of the series receiving seven inunctions of gray ointment but was present in the others. There was a mild swelling of the vascular endothelium. The pia arachnoid contained an occasional infiltrating round cell, but no distinct groups of such cells were present.

An indistinct conglutination of erythrocytes was found. The ganglion cells did not present any distinct alteration.

Heart.—No alterations which can definitely be attributed to the medication were found, the organs being apparently of normal structure.



Fig. 25.—Rabbit; eighteen inunctions with mercurial ointment (gray ointment). Kidney: Shrinkage of the epithelium of the convoluted tubules because of fatty "degeneration." The lumina are filled with granular, eosin-staining debris.

Lungs.—There was well marked congestion accompanied by mild edema; the degree varied with the amount of medication. The distended alveolar capillaries contained an increased number of polymorphonuclear leukocytes; which was regarded as not being the result of the kind but of the mode of medication because of cutaneous infection due to irritation. The bronchi and pleurae were normal. Con-

siderable conglutination and partial hyalinization of erythrocytes were present. No appreciable quantity of hemosiderin was found.

Spleen.—In the first animal of this group congestion constituted the only discernible lesion. In the animals which received more treatment the blood spaces were widely distended with erythrocytes, many of which were degenerating, shadow forms being frequently seen; conglutination was likewise frequently found. Hemosiderin containing phagocytes occurred in moderate numbers with moderate quantities of free hemosiderin in the tissue. A number of phagocytes contained black granules which may be particles of mercury. Such granule containing cells were also sometimes found in other series, usually in the spleen or liver, but never as distinctly as in these tissues. (Chemical studies of their nature were not undertaken.) The pulp cords were thinned in proportion to the vascular engorgement. Foreign cells were not present. The trabeculae and the fibrillar framework appeared unaltered.

Liver.—There was an inconspicuous periportal connective tissue proliferation and small round cell infiltration; the bile ducts appeared normal. The sinusoids were moderately engorged; the erythrocytic alterations were not marked.

The Kupfer cells were slightly swollen and many contained small black amorphous granules. The liver cells generally appeared normal or were slightly more granular. Practically no hemosiderin was found.

Kidneys.—The alteration here varied in proportion to the number of inunctions. In the first animal cloudy swelling involving particularly the convoluted tubules was present; the tubular lumena were often entirely occluded by the swollen, granular and sometimes anuclear cells. The straight tubules were slightly involved while the large collecting tubules showed no cellular lesions; hyaline or granular casts were sometimes found. The intertubular capillaries were frequently compressed by the enlarged tubules; the glomeruli filled about three fourths of the capsular spaces, which now and then contained eosin-staining smooth or finely granular material.

The animals which received seventeen and eighteen inunctions showed granular cells in the convoluted tubules; but these cells were usually no longer swollen and were even decidedly shrunken (Fig. 25). The widened tubular lumena were usually partly filled with eosin-staining structureless material sometimes appearing like small hyaline droplets.

In these later cases a moderate engorgement of the intertubular as well as glomerular capillaries was present. There was no connective tissue proliferation or calcification.

Suprarenals.—The suprarenal glands showed no alterations from the normal.

II. HISTOLOGIC CHANGES PRODUCED BY THE INUNCTION OF CALOMEL OINTMENT

Cerebrum, Cerebellum, Brain Stem and Meninges.—In none of the various sections examined was there any perivascular infiltration; the meninges appeared normal and there were no notable blood vascular changes. The ganglion cells were likewise seemingly unaltered.

Heart.—This organ appeared practically normal. There was an occasional swollen muscle fiber with poor striations and a few vacuoles; but generally the muscles stained well and appeared normal. Cellular infiltrations were not seen. The interstitial tissue, the vessels and the heart coverings were normal.

Lungs.—In one animal a terminal bronchopneumonia was found; the other two possessed practically normal lungs. In the rabbit which received twenty-four treatments a few vessels contained hyaline material and conglutinated erythrocytes. Hemosiderin was not present. The bronchi, lung tissue and the pleural surfaces were normal.

Spleen.—There was a moderate engorgement, and in the animal which received the largest number of treatments, a mild hemosiderin pigmentation was found. Some phagocytic cells also contained minute black amorphous granules; a moderate degree of erythrocytic degeneration was present. The malpighian follicles were of average size and occasionally contained prominent centers. The pulp cords, reticular tissues, trabeculae and capsules appeared normal.

Liver.—The periportal tissue was normal in all of the animals. There was a moderate engorgement, particularly in the rabbit which had received twenty-three treatments, and some conglutination of the erythrocytes was noted. A few swollen Kupfer cells contained small black amorphous material. The liver cells appeared slightly granular, but otherwise normal. There was no excess of hemosiderin.

Kidneys.—More or less marked parenchymatous degeneration, particularly of the convoluted tubules, was found. The cell changes here varied from increased granularity to swelling, vacuolization, nuclear degeneration, necrosis and desquamation. Plugs of hyaline or granular structureless material were present in almost every tubule. The straight and collecting tubules presented little cellular involvement. The glomeruli were moderately engorged, filled about three fourths of the capsular spaces and were apparently normal. The capsular linings were slightly swollen and an occasional desquamated cell or some eosin-staining debris were present in the capsular spaces. Bowman's cap-

sules were of normal thickness. The intertubular capillaries were moderately engorged, but in some places they were compressed by the tubular swelling. Connective tissue proliferation did not occur.

Suprarenals.—The suprarenal glands showed no discernible changes.

GENERAL SUMMARY OF THE HISTOLOGIC CHANGES PRODUCED BY COMPOUNDS OF MERCURY

As expected, individual animals exhibited varying degrees of tissue injury, so that a comparison of the kind and severity of the lesions produced by the different preparations of mercury administered by different routes, in multiple small doses, is possible only in a broad and general manner.

The lesions produced by the different mercurials were quite similar and may be briefly summarized for the different organs.

Brain and Meninges.—These tissues showed an interesting and unexpected perivascular round cell infiltration; curiously this change is regarded as more or less constant in syphilitic infection of these tissues, and our findings quite naturally raise the question of the significance of perivascular round cell infiltration in the brain of syphilitic subjects who have taken mercury during life. At the present time we are continuing our investigations with monkeys in order to shed further light on this and other interesting histologic changes due to the administration of mercurial compounds.

Among the animals receiving a large amount of mercury, some congestion and edema with slight perivascular round cell infiltration were noted in the pia mater. These lesions were somewhat more marked in animals which received intramuscular injections.

Heart.—As a general rule, this organ showed no changes although among those animals receiving the maximum amounts of mercury there were evidences of slight focal necrosis of the muscle cells with intermuscular round cell infiltration. Occasionally the capillaries contained masses of conglutinated and hyalinized erythrocytes.

Lungs.—Changes in the lungs when found at all, mainly consisted of congestion and slight edema. It was of considerable interest to find that the erythrocytes were frequently conglutinated and hyalinized, resembling the changes found in the lungs of rabbits after the administration of arsphenamin.

Spleen.—The changes found in this organ consisted mainly of hyperemia and hemosiderosis, apparently due to increased blood destruction as the result of the administration of the different preparations of mercury.

Liver.—Changes in the liver were usually inconspicuous and when noted at all comprised congestion, filling of the sinusoids with partially hemolyzed erythrocytes and hemosiderin staining of neighboring hepatic cells. In some animals there were evidences of slight cloudy swelling of the hepatic cells and slight perilobular fibrosis.

Kidneys.—These organs have shown the most conspicuous changes analogous to those previously described² and every one showed some degree of tissue injury, the severity varying considerably according to the amount of mercury administered.

The most constant lesions were found in the tubules characterized by cloudy swelling, fatty degeneration, frank necrosis, calcareous infiltration and the presence of large numbers of casts. The convoluted tubules suffered most; the limbs and loops of Henle were sometimes involved while the collecting tubules generally escaped.

The glomeruli were sometimes hyperemic and among animals receiving the larger amounts of mercury, granular exudates occurred in the capsular spaces.

Among the animals surviving for the longer periods of time, there were evidences of repair of the tubular cells accompanied by interstitial changes of lymphocytic infiltration and fibrosis.

Suprarenal Glands.—As far as we could ascertain with hematoxylin and eosin-stained sections these organs showed no changes although we report reservedly on the histology of these tissues in this series of experiments.

Unfortunately and in an unexplainable manner, we overlooked extending our studies to the gastro-intestinal tracts of these experimental animals for the evidences of necrosis found by other investigators in mercurial intoxication produced by corrosive sublimate.

THE RELATION OF THE KIND OF COMPOUND OF MERCURY AND ROUTE OF ADMINISTRATION TO TISSUE INJURY

A comparison of the histologic changes induced by the intramuscular, intravenous and oral administration of the different preparations of mercury employed in this study indicates that in general terms the severity of the tissue injuries and notably that of the kidneys, bears a more or less direct relationship to the amount of pure mercury administered. These amounts have been calculated and are shown in the tables. As previously shown by Schamberg, Kolmer and Raiziss,² the same condition prevails relative to the toxicity of the various preparations of mercury as judged by the duration of the lives of rabbits, the toxicity being directly proportionate to the amount of pure mercury administered.

This certainly appears to be true when the compounds of mercury are injected intravenously and intramuscularly. Probably the same is true as regards the effects produced by inunctions of mercury and administration by mouth, that is, the toxicity as measured by the duration of life and degree of tissue injury is in direct proportion to the amount of pure mercury absorbed irrespective of the preparation of mercury administered, although variation in the duration of the lives of experimental animals and the degrees of tissue injury are more apt to occur when mercury is administered by these routes due, probably, to variation in absorption of mercury.

CONCLUSIONS

1. The administration to rabbits of different soluble and insoluble mercurial compounds commonly employed in the treatment of syphilis, by intramuscular and intravenous injection, inunction and oral administration, and in amounts analogous to the maximum doses given to human beings, resulted in the production of tissue changes in all organs examined, namely, the brain, heart, lungs, spleen, liver and kidneys.

2. The most conspicuous changes were found in the brain in the nature of perivascular round cell infiltrations, and in the kidneys, as tubular and capsular glomerulonephroses of varying degrees of severity. Details of the histologic changes in these and the other organs included in this study are described.

3. The degree of tissue injury caused by the different preparations of mercury appears to bear a direct relation to the actual amounts of pure mercury absorbed irrespective of the kind of preparation and route of administration.⁵

CLINICAL COMMENTARY ON STUDIES OF HISTOLOGIC CHANGES IN ORGANS INDUCED BY ARSPHENAMIN, BY NEO-ARSPHENAMIN AND BY MERCURY

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The elaborate studies carried out by my colleagues, Drs. Kolmer and Lucke, on the histologic changes produced in the organs of experimental animals by arspnenamin, by neo-arsphenamin and by mercury are of interest and importance.

Scientific therapeusis presupposes a definite knowledge not only of established clinical results but likewise of the pharmacologic and toxicologic effects of remedies. A prolific literature has grown up on the clinical aspects of arspnenamin and neo-arsphenamin, but our knowledge of the pharmacology and toxicology of these complex compounds, as well as their fate in the human economy, is far from complete.

One of the fundamental principles of the new science of chemotherapy is that a chemical compound in order to be of practical value in the treatment of an infectious disease must have a greater affinity for the parasite than for the body cells, and the greater the discrepancy, the more valuable is the drug. In other words, there should be a large latitude of safety between the *dosis therapeutica* and the *dosis toxica seu lethalis*.

All powerful drugs doubtless bring about some structural changes in the cells of certain organs. When these structural changes are minimal no material interference with the integrity of function is induced. Where, however, severe or massive damage results organic insufficiency may be brought about, in some cases to such an extent as to lead to a fatal result.

In considering the structural changes induced by therapeutic doses of arspnenamin, neo-arsphenamin and mercury, we must remember that many infectious diseases likewise induce structural changes and organic restitution takes place. Influenza, typhoid fever and other infections may, for example, produce focal necroses in the liver, without ultimately interfering with proper functioning of that organ. Other infections, notably scarlet fever, may cause severe changes in the kidney, and yet restoration to healthy activity commonly results. It is well, however, to know what organs bear the brunt of the attack

when these powerful drugs are administered in order that we may watch symptoms referable to these organs and thus intelligently guide ourselves in the treatment. It should not be forgotten that in the treatment of a difficult disease like syphilis prolonged treatment is necessary and repeated organic insults, unless carefully watched, may lead to unfortunate results.

CLINICAL EXPERIENCE AND PATHOLOGIC FINDINGS

Let us consider to what extent clinical observation corresponds with the microscopic studies here discussed in elucidating the toxicologic effects of arsphenamin, neo-arsphenamin and mercury.

The studies carried out by Kolmer and Lucke indicate that the arsphenamins produce demonstrable effects chiefly on the liver, suprarenals and the blood vessels, and mercury chiefly on the kidneys and brain. The arsphenamins would appear to have a special affinity for the organs referred to—a hepatotropism, an adrenotropism and a vasculotropism. Mercury possesses a nephrotropism (an observation long known) and apparently a cerebrotropism, an observation which is as far as we know, new.

Do these biochemical affinities throw any light upon the toxic phenomena following the use of these drugs?

Space will not permit a discussion of the various reactions which from time to time follow the use of the arsphenamins. A large literature has already accumulated on this vexed subject. To mention briefly only the immediate nitroid reactions conjures up to the considerable diversity of opinion on the causation of these phenomena. Within the scope of this communication it might be pertinent to inquire whether the influence on the suprarenals and the chromaffin cells observed by Kolmer and Lucke, might bear any relationship to some of the symptoms of the nitritoid reaction. The most characteristic phenomenon of this syndrome is a pronounced vasoparesis followed in some cases by a great fall of blood pressure.

May this not in some cases be due to an inhibition of the production or secretion of epinephrin? It is not suggested that these reactions are usually due to the effect of the drug on the suprarenals, but the fact cannot be denied that suprarenal suppression might induce a similar picture.

Most of the fatalities following the use of the arsphenamins may be grouped under two heads—those referable to the liver and those affecting the brain and its membranes.

Kolmer and Lucke have shown that the arsphenamins in therapeutic dosage may induce slight structural changes in the liver and that huge

doses, such as are used to test the drug on animals, may cause quite considerable focal necroses. Warthin¹ says: "It is worthy of note that in a case of secondary syphilis dying of salvarsan poisoning focal necroses containing spirochaetes were present throughout the liver." In this connection the whole subject of jaundice in syphilis becomes pertinent for discussion. Without entering exhaustively into the subject it may be said that there are several types of jaundice observed in syphilis: (a) true syphilitic jaundice, appearing before any treatment has been begun and due doubtless to a diffuse degeneration of the liver cells produced by *Spirochaeta pallida*; (b) jaundice due to the combined effect of hepatic syphilis and arsenical treatment (in these cases the jaundice is a sort of Herxheimer reaction); and (c) jaundice due to structural changes in the liver induced by the arsenicals and going on in some cases to the development of acute yellow atrophy.

It is a significant fact that jaundice is much more commonly observed in syphilis now than before the introduction of arsphenamin. Osler found jaundice in syphilis (before arsphenamin) in 0.37 per cent. of cases. Harrison² found jaundice in 0.6 per cent. of cases of syphilis during or subsequent to arsenical treatment. Ravaut reports twenty cases of jaundice in patients receiving 94,672 injections of various arsphenamins. Scott and Pearson³ observed thirty-nine cases among 13,664 arsenical injections. Bailey and MacKay⁴ studied twenty-five cases of toxic jaundice developing in patients receiving arsenical and mercurial treatment. Silbergleit and Föckler⁵ report that they observed thirteen cases of acute yellow atrophy of the liver, all fatal, and all occurring in syphilitic patients who shortly before had been given mercurial and neo-arsphenamin treatment.

It can no longer be contested that jaundice and acute yellow atrophy are much more common nowadays than before the introduction of the arsphenamins. Nevertheless, we find a high incidence of such complications in certain countries and in the hands of certain clinicians and a low incidence elsewhere.

Is there any explanation for the discrepancy in the incidence of this complication? The writer believes that there is. In my own clinic in the Polyclinic Hospital (Graduate School of Medicine of the University of Pennsylvania) over 12,000 injections of the arsphenamins have been given, and we have only observed three cases of jaundice.

1. Warthin: Am. J. Syphilis **2**:445 (July) 1918.

2. Harrison: Quart. J. Med. **40**:321 (July) 1917.

3. Scott and Pearson: Am. J. Syphilis **3**:629 (Oct.) 1919.

4. Bailey, C. V., and MacKay, A.: Toxic Jaundice in Patients Under Anti-syphilitic Treatment, Arch. Int. Med. **25**:6286 (June) 1920.

5. Silbergleit and Föckler: Ztschr. f. klin. Med. **88**:333, 1919.

Furthermore, we have only encountered two mild cases of exfoliative dermatitis, a condition which is essentially an expression of arsenical intoxication.

What is the explanation of this low incidence of jaundice and exfoliative dermatitis? I believe it to be due to the fact that, for purposes of scientific investigation, our treatment of syphilis is an exclusive arsenical treatment. We are studying the effect of arsphenamin and neo-arsphenamin on syphilis, and we do not complicate this study by administering mercury. The arsenical treatment is fairly vigorous, patients receiving two 0.4 gm. doses of arsphenamin or two 0.9 gm. of neo-arsphenamin twice a week. Some patients have had this treatment continued until fifteen or twenty treatments have been given without interruption. We have never encountered a case of yellow atrophy of the liver or of encephalitis. In my private practice treatment has at times been much more intensive than that indicated above, and yet no hepatic, cerebral or cutaneous complications have occurred. I am of the opinion that conjoint mercurial and arsphenamin treatment, while perhaps more curative, is more liable to complications and fatalities. Some clinics in which mercury and arsphenamin are conjointly used encounter jaundice and dermatitis far more commonly than we do.

Wechselmann⁶ says: "My entire experience with more than 25,000 injections forces me to conclude that salvarsan is much less toxic than mercury. My department in which salvarsan is used almost exclusively has given me much less care and trouble during the past three years than in the previous period when mercury was employed."

A remarkable and unfortunate series of cases of "Delayed Arsenical Poisoning" is reported by Strathy, Smith and Hannah.⁷ They describe fifty-eight cases of late arsenical poisoning, eight of which were fatal, the symptoms developing, on an average, forty-three days after the last arsenical treatment. Jaundice was the most prominent symptom, being present in all of the fatal cases and in thirty-nine of the nonfatal group. There were also eight cases of exfoliative dermatitis. The writers state that "intensive treatment" was used, i. e., doses of arsphenamin and mercury, each once a week for seven or eight weeks. Intramuscular injections of mercurial oil (gray oil) were given at the same time as the arsenical treatment. Nearly all of the patients were treated with foreign makes of neo-arsphenamin. The patients were all between 20 and 40 years of age. Necropsy examinations in most

6. Wechselmann: *The Pathogenesis of Salvarsan Fatalities*, trans. 1913, St. Louis, p. 106.

7. Strathy, Smith and Hannah: *Lancet*, April 10, 1920, p. 802-807.

of the cases exhibited changes in the kidneys, in addition to hepatic atrophy. The greatest total amount of arspenamin used in any case was less than 7 gm. and the least amount 2.2 gm. These cases in all probability represent arsenical poisoning due to the vigorous conjoint use of mercury and arsenic. The authors themselves suspected this for they say: "A few of the patients showed slight symptoms of mercurial poisoning, but mercury is known to be an irritant of the kidneys and in excessive doses to cause degeneration of the tubular epithelium, and it seems not at all unlikely that for this reason it acted as a predisposing factor.

The pathogeny of such poisonings is reasonably clear. Mercury in vigorous dosage, particularly when the insoluble salts are used, may severely irritate the kidneys and inhibit their power to eliminate arspenamin. Within a short time after an injection of arspenamin most of it disappears from the blood and is lodged in the organs, one of the chief reservoirs being the liver. If the eliminatory activity of the kidneys is impaired, it is obvious that the arspenamin will remain for a longer time and in larger quantities in the liver, for which organ it has a considerable affinity. Too long a residence in the liver may cause the drug either to become oxidized with the production of arsenoxid, or the arsenical radical may become split off and produce the symptoms of arsenical poisoning.

The Salvarsan Committee, appointed by the British Medical Research Council, in its first report referred to some outbreaks of toxic jaundice, attended by a high fatality, which occurred in certain military hospitals after the use of the organic arsenicals. At the suggestion of the committee, Dr. H. M. Turnbull made an examination of the tissues from eight fatal cases. He concludes that "the liver in all cases was the site of a severe pathologic lesion, a lesion more severe than that in any other organs. . . . The liver was the seat of severe degeneration and necrosis.

"The kidney was available for examination in six cases, and in all showed a severe parenchymatous degeneration." No true nephritis was present. Turnbull regarded the kidney changes as secondary.

COMPARATIVE EFFECT OF ARSPHENAMIN AND NEO-ARSPHENAMIN

While the studies of Kolmer and Lucke indicate that similar structural changes occur after the use of arspenamin and neo-arsphenamin, they call attention to the fact that the changes are distinctly less severe after neo-arsphenamin. This finding is in harmony with clinical observation. It may be definitely stated that neo-arsphenamin has less than one half the toxicity of arspenamin and is unquestionably a safer remedy. This is due in part to the fact that one of

the anchoring groups—amino group—is closed, and furthermore, to the fact that neo-arsphenamin is neutral in reaction and does not in ordinary concentration produce hemolysis.

The studies under discussion indicate that the most damaging solutions of arsphenamin are acid solutions, an observation fully confirmed by the tragic results of inadvertently administered solutions of unneutralized arsphenamin in the human subject.

It is probable, however, that the vascular injuries described by Kolmer and Lucke are not solely due to solutions of strong hydrogen-ion (acid) concentration on the one hand nor to strong hydroxyl-ion (alkaline) concentration on the other, as similar although milder changes are observed after the use of neo-arsphenamin. It is possible that such changes are in considerable part arsenical in origin.

STRUCTURAL CHANGES INDUCED BY MERCURY

It has long been known that mercury has an affinity for the kidneys and that mercurial poisoning is apt to be associated with a nephritis. Accidental poisoning with mercuric chlorid kills in this manner.

The studies of Kolmer and Lucke are interesting in that they demonstrate that relatively short courses of mercury may produce perceptible renal changes. Even in rats that received treatment by mouth for from four to six weeks recognizable changes were observed in certain organs. These rats received 2 mg. (1/30 grain) of yellow mercurous iodid a day. This would correspond to 2 grains daily for a man weighing 130 pounds. This is somewhat larger than the ordinary therapeutic dose but not greater than the old method of administering an increasing number of pills daily until "some characteristic toxic effect of the drug is produced."

This dosage in rats caused slight structural changes in the spleen, liver and heart, but more pronounced alterations in the brain and kidneys. Remarkable to relate, a distinct perivascular cell infiltration was observed about the vessels of the brain. This was seen in all of the animals treated sufficiently long with mercury, no matter how administered, but was never observed in animals treated with arsphenamin. As far as we know, this observation of Kolmer and Lucke has not been hitherto recorded. In order to determine whether animals of a higher species will exhibit similar changes, experiments are now being carried out on monkeys.

The kidneys of rats receiving yellow mercurous iodid for from four to six weeks showed hyaline and granular casts in the collecting tubules. Vacuolated epithelial cells and cellular shrinkage were observed in the convoluted tubules, and there was mild connective tissue proliferation.

More pronounced kidney damage was seen in the animals receiving more vigorous treatment by inunction, intramuscular or intravenous treatment. The channel of introduction of the drug did not appear to be a determining factor, nor the form of mercury used. The structural alterations were proportional to the amount of the drug in terms of pure mercury absorbed into the blood stream.

GENERAL DISCUSSION

Both the arspenamins and mercury administered in therapeutic doses bring about some structural alterations in organs. These are doubtless ordinarily repaired like the changes that take place in various acute infectious diseases. The chief organs affected by the arspenamins are the liver, the suprarenals and the blood vessels. The effects of mercury, on the other hand, are seen dominantly in the kidneys and in the brain. The pathologic findings and clinical experience would alike persuade one to utter two cautions: In mercurial treatment watch the kidneys; in arspenamin treatment watch the liver. To be sure, as stated by Milian, in early syphilis jaundice may indicate either hepatic syphilis or a Herxheimer reaction, and will respond to more vigorous treatment when the less intense treatment has failed. Later in the disease, however, and particularly after the vigorous use of the arsenicals, the development of jaundice should lead to a suspension of all specific treatment. The treatment of syphilis requires the repeated use of these drugs. When used with circumspection and good judgment harmful results may in large part be avoided. When used unskilfully, without proper examination of the patient and without knowledge of warning signals, unfortunate results may take place. The fact should be emphasized that the body tolerates much larger amounts of arspenamin than mercury. One may, for instance, administer intravenously to a white rat, fifty times as much arspenamin as mercury. More mercury cannot be administered because it has too great an affinity for body cells. The therapeutic dose of arspenamin is infinitely more destructive to the spirochete of syphilis than the therapeutic dose of mercury. The spirochetes in a chancre can be destroyed in a few hours by an injection of arspenamin; this accomplishment is impossible with a single injection of mercury. Fatalities have occurred both after arspenamin and mercury. Those after the former are much more tragic and fear inspiring, for the relation between cause and effect is obvious. Many scores, if not hundreds, of deaths after mercury have likewise been reported in the literature, but they are ordinarily more apt to be slow and insidious and less likely to be incriminative of the therapeutic procedure employed.

In conclusion, the writer cannot refrain from expressing his opinion that vigorous mercurial treatment is often responsible for arsenical intoxication when arsphenamin and mercury are used at the same time. Large doses of both ought not to be employed synchronously. When the two are used jointly their respective dosages should be inversely proportional to each other. It would appear best to give the courses of mercury subsequent to that of arsenic.

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THE ETIOLOGY OF ECZEMA

WITH A PRELIMINARY REPORT OF EXPERIMENTAL STUDIES*

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CHICAGO

It has been the custom of the Chicago Dermatological Society to penalize the retiring president to the extent that his "swan song" shall consist of a paper on some subject of dermatologic interest. Conforming to that custom, I offer the following remarks on the etiology of eczema. It might be well here to ask the indulgence of the Society and its friends for taking up their time with a discussion on such a commonplace subject. My only excuse for so doing is that since the selection of the subject is left to the victim I can say that I know of no other dermatosis that plays such a large part in the life of the dermatologist nor one an adequate explanation of which would have a greater influence on his conceptions of many cutaneous diseases.

With the controversy over the relative merits of the terms dermatitis and eczema I shall have nothing to do. In my mind that question will be settled when we find the etiology of the latter.

The various theories as to the causation of eczema may grossly be divided into three classes: external irritation, bacterial irritation, and

* This paper, published posthumously under an improvised title, is a fragment which I believe all who cherish the memory of Frederick G. Harris will be glad to see in print. The address was delivered in January, 1916, as that of the retiring president of the Chicago Dermatological Association. I was so much impressed with the point of view of the thesis itself and with the originality of approach and the promise of the experimental work that I repeatedly urged publication on its author while he lived, and after his untimely passing, could not rest content until I had, through Mrs. Harris' cooperation, unearthed the manuscript. The bibliography alone, of which unhappily only a remnant was found, represents, so Mrs. Harris informs me, many months of intensive reading. No evidence of any collaborative assistance could be found in the available papers. My personal hand in the matter extends to the improvising of a title, the checking of as many bibliographic references as possible, the correction of a few obvious stenographic errors in what must have been a first draft, the interchanging of one or two paragraphs, the insertion of subtitles, and the summarizing of one chart (b-imidazoletethylamin determinations).

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humeral irritation, according as their adherents, while admitting other factors, place the most weight on the one or the other.

The external irritation theory is fathered by the Vienna school beginning with Hebra; to this school, external irritation, mechanical, chemical or thermal, is the important factor in the production of the disease.

The infectious theory is represented by the Hamburg school. Here the all important cause is held to be the various pyogenic cocci. It would seem that this view has the least to recommend it, for it has been shown repeatedly that the fresh eczema vesicle is sterile. Bruck and Hidaka¹ studied the subject biologically and were unable to demonstrate an increase in agglutinin or hemolysin. Bering and Enomoto² showed that the scales of eczema contained no increase of opsinin over those of other dermatoses. Their results with agglutinin were similar to those of Bruck and Hidaka. We must admit that after an eczema is once established, bacteria may play an important part as an irritant and serve to prolong the disease, but as for their being the exciting factor, except in rare cases the theory would seem to have little to recommend it.

The internal or humeral theory is represented by the French school.

The writer has long felt that the important factor in the production of an eczema was an increased irritability of the skin or of some structure in it, this abnormal irritability resulting in a reaction of the skin to irritants of varying degrees of intensity. Thus a skin in this state of unstable equilibrium would react to an irritant of any type, be it ever so mild. A skin in a state of normal equilibrium would require an irritant of great intensity, the reaction in this case being called an artificial dermatitis. A skin in a highly irritable state could react to a stimulant so mild as to be considered physiologic.

There are many facts, clinical and experimental, which serve to substantiate this view of the etiology of eczema. The treatment of the disease would be greatly simplified if we knew the factor or factors which are capable of upsetting the normal equilibrium. With that object in view this study was undertaken, and it is to be considered in the nature of a preliminary report.

REVIEW OF THE LITERATURE

In 1892, Samuel³ showed that after a rabbit's ear had recovered from a croton oil dermatitis, the skin of that area was relatively immune

1. Bruck, C., and Hidaka, S.: Biologische Untersuchungen über die Rolle der Staphylokokken bei Ekzemen, *Arch. f. Dermat. u. Syph.* **100**:165-176, 1910.

2. Bering and Enomoto: Zur Aetiologie des Ekzems, *Arch. f. Dermat. u. Syph.* **119**:365-367, 1914.

3. Samuel, S.: Ueber eine Art von Immunität nach überstandener Croton-Entzündung, *Arch. f. path. Anat. u. Physiol. u. f. klin. Med.* **127**:467-476, 1892.

to a second application. This immunity lasted from four to five weeks and could be kept up indefinitely by continued intermittent applications. He showed that the inflammatory reaction in the immunized ear was less and of shorter duration than was the case in a normal ear. He was able to prevent inflammation of one ear by dipping the other ear in cold water, showing the influence of the nervous system on the production of inflammation.

Schaer ⁴ produced a similar immunity with croton oil too weak to cause more than the mildest grades of dermatitis.

Fuerst ⁵ studied the changes of the epithelium caused by heat and cold in men and animals. He was able by repeated freezing or burning to so change the skin that the same exposures caused no inflammatory reaction.

Stein,⁶ using applications of croton oil, ethyl chlorid and carbon dioxid snow, of increasing strength, but short of those required to produce a visible dermatitis, was able to produce an immunity which was not specific, but which was of longer duration, and more marked for the specific agent. He says that this immunity is not due to anatomic changes, but is due to changes in the cells of the affected tissues (cellular umstimmung). It is a common occurrence to see patients with pediculosis whose skin seems to have an immunity to the traumatism of scratching. The result of scratching in this disease is usually a pus infection, not an eczema. It is difficult to correlate these observations with the numerous cases of acute eczema of sudden onset, seemingly due to an irritant to which the patient has been exposed often for years.

Schultz,⁷ in a series of careful experiments on patients suffering with various diseases, has studied the reaction of the normal skin of these patients to decreasing strengths of phenol. Some of his findings are interesting and significant. He showed that there was no constant difference in the reaction of the skin in different parts of the body of the same person. The age of the person, moreover, had no influence on the reaction. The skin of forty-one syphilitic patients reacted in about the same way as that of normal persons. One syphilitic patient showed an increased reaction, but it is interesting to note that this was in a fat man with a tendency to intertriginous eczema.

4. Unable to trace.

5. Fuerst, E.: Ueber die Veränderungen des Epithels durch leichte Wärme- und Kälteeinwirkungen beim Menschen und Säugethier, Beitr. z. path. Anat. u. allg. Path. **24**:415-457, 1898.

6. Stein, R.: Experimentelle und histologische Untersuchungen über Hautgewöhnung, Arch. f. Dermat. u. Syph. **97**:27-54, 1909.

7. Schultz, J. H.: Die Prüfung der Hautreaktion auf chemische Reize, Jahrb. f. Kinderh., N. S. **78**:347-349, 1913.

Normal areas of skin in psoriatic patients showed less reaction than the skin of persons free from psoriasis. One psoriatic patient showed an increased reaction. It is noted, however, that this patient was so susceptible to chrysarobin that it was necessary to stop the treatment from time to time. Patients with ichthyosis and dermatitis herpetiformis gave a decreased reaction. Normal skin of eczema patients showed a remarkably increased reaction.

Weidenfeld⁸ made an extensive study of the reaction of the skin of eczema patients to irritants, using decreasing strengths of croton oil. Although his results run parallel to those of Schultz, we believe it worth while to give some of his findings in detail. He found that the skin of eczema patients shows a greater reaction than normal skin, and the more acute the disease the stronger is the reaction. As a rule, the more extensive the disease is, the greater is the reaction. The strength of the reaction, as a rule, decreases as the disease disappears. The increased sensitiveness lasts for some time after recovery, but is, however, transitory. The normal skin near the eczematous patch shows a greater reaction than that at a distance. The skin of a healed patch is more sensitive than the skin that has not been affected. The serum of eczema patches, applied to intact skin or to skin which had been scarified, does not cause eczema. Scarification and application of croton oil showed eczema patients to be much more sensitive than normal persons. Ichthyotic skins showed a lessened reaction.

Kaposi,⁴ Kreibich⁹ and others hold that under the influence of the primary patch of eczema the vasomotor system of the whole skin is irritated.

Weidenfeld thinks that the irritability of the whole skin runs so parallel to that of the primary patch that no other conclusion is permissible than that in the primary patch, toxic substances are formed which pass into the blood and cause those changes in the skin which predispose it to eczema.

Rachmilewitsch¹⁰ has shown that the skin of children with exudative diatheses is more sensitive to mechanical and chemical irritation than that of normal children.

All these experiments would seem to indicate that the skin in eczema is in an unstable condition, ready to respond to the slightest irritant by the production of an inflammatory reaction which we call eczema.

8. Weidenfeld, S.: Beiträge zur Pathogenese des Ekzems, *Arch. f. Dermat. u. Syph.* **111**:891-984, 1912.

9. Kreibich, C.: Ueber nervöse Ueberempfindlichkeit der Haut, *Arch. f. Dermat. u. Syph.* **93**:59-64, 1908.

10. Rachmilewitsch, E.: Hautreaktionen von Kindern mit exudativer Diathese, *Jahrb. f. Kinderh., N. S.* **77**: 176-180, 1913.

That this irritability does not reside in the epithelial cells is shown by the fact that it is not specific, and it varies too rapidly. Weidenfeld showed, moreover, that subepidermal injection of croton oil in eczema gave an increased reaction. The source of the irritability could reside in the blood vessels or nerves. There are many reasons for believing that the blood vessels are only secondarily involved. Therefore it might be well to investigate the possibility that the nervous system is at fault.

INFLUENCE OF THE NERVOUS SYSTEM ON DERMATOSES

There are a number of dermatoses, in the etiology of which the nervous system is supposed to play a greater or less rôle. Cassirer,¹¹ who is probably the best authority on the question of neurotropism, has pointed out that the skin is especially well suited for the demonstration of neurotrophic changes.

Königstein¹² has called attention to the sensory changes present in vitiligo patches, the center being hypesthetic, while the border is hyperesthetic.

Kreibich had previously shown that the border of a patch of vitiligo reacts much more strongly to irritation than does the center. Schultz, in the phenol experiments referred to in the foregoing, found in three vitiligo cases with sensory changes, that the reaction was increased at the periphery and decreased in the center. Two cases without sensory changes gave normal reactions. Vörner⁴ has verified these observations.

It is interesting to learn that Moro⁴ believes that his tuberculin reaction, which clinically simulates eczema rather closely, is an inflammatory reaction due to the irritation of nerves sensitized to tuberculin.

In 1906, Spiess¹³ reported some observations and experiments which have not received the attention they would seem to deserve. He noticed that after tonsillectomy, if the denuded area was anesthetized, the inflammatory reaction and swelling was distinctly less or absent, and the wound healed more quickly. He found that various drugs, such as morphin, antipyrin, salicylic acid and quinin given internally had a similar action.

Spiess here calls attention to an every-day occurrence as showing the influence of the nervous system on the manifestations of inflammation. He cites the fact that a rhinitis, the secretion of which is profuse during the day, stops during sleep. He mentions also that wounds in

11. Cassirer, R.: Die trophischen Störungen, *Handb. d. Neurol.* **1**:1135-1156, 1910.

12. Königstein, H.: Sensibilitätsstörungen bei Vitiligo, *Wien. klin. Wchnschr.* **23**:1745-1748, 1910.

13. Spiess, G.: Die Bedeutung der Anästhesie in der Entzündungstherapie, *München. med. Wchnschr.* **53**:345-351, 1906.

hysterical and insane patients heal readily with few inflammatory signs. Strümpel¹⁴ reports the case of an hysterical woman who could pick eggs out of boiling water without showing burns. From his experiments Spiess concludes that an inflammation will not occur when one succeeds in anesthetizing the reflex fibers passing from the area in the sensory nerve.

In Samuel's experiments, he showed that when the sensory nerves supplying the ears of rabbits were cut, scalding did not cause inflammation. There are many other clinical observations showing the influence of the nervous system on inflammation (lepra, syringomyelia). The observations of Samuels and Spiess have been abundantly confirmed by the experiments of Bruce,¹⁵ Januschke,¹⁶ and Luithlen.¹⁷

Bruce showed that when the conjunctiva was anesthetized with alypin or by cutting its sensory nerves, the instillation of oil of mustard into the conjunctival sac was not followed by inflammation.

Januschke found that magnesium sulphate narcosis, also narcosis with chloral hydrate or ether, delayed or prevented inflammatory reactions. Morphin, antipyrin, sodium salicylate and quinin exhibited the same effect, but to a less extent. He also found, and this I wish especially to emphasize, that epinephrin subcutaneously administered also prevented the usual inflammatory reaction, and this is spite of the fact that there was no appreciable influence on the blood vessels.

Weidenfeld¹⁸ has shown that in cases of dermographism, the skin did not react over an area anesthetized with cocain, and that epinephrin influenced the skin in such a way that it did not react to mechanical irritation. He also showed that epinephrin applied either externally or subcutaneously, would prevent the inflammatory reaction to mustard

14. Strümpel: Quoted by Spiess.

15. Bruce, A. N.: Ueber die Beziehung der sensiblen Nervenendigungen zum Entzündungsvorgang, *Arch. f. exper. Path. u. Pharmacol.* **63**:424-433, 1910; abstr. *Arch. f. Dermat. u. Syph.* **107**:508-509, 1911.

16. Januschke, H.: Ueber Entzündungshemmung, *Wien. klin. Wchnschr.* **26**: 869-874, 1913.

17. Luithlen, F.: Tierversuche über Hautreaktion, *Wien. klin. Wchnschr.* **24**:703-705, 1911. Ueber Chemie der Haut, *Wien. klin. Wchnschr.* **25**:658, 1912. Ueber die Einwirkung parenteral eingeführter Kolloide und wiederholter Aderlässe auf die Durchlässigkeit der Gefäße, *Med. Klin.* **2**:1713-1714, 1913. Ueber Veränderungen der Hautreaktion, *Wien. klin. Wchnschr.* **26**:1836-1837, 1913. The Etiology and Etiologic Therapy of Eczema from a Chemical Basis, *Urol. & Cutan. Rev., Tech. Suppl.* **1**:97-101, 1913. Veränderungen der Hautreaktion bei Injektion von Serum und kolloidalen Substanzen, *Wien. klin. Wchnschr.* **26**:653-658, 1913. Ueber Allgemeinbehandlung der Hautkrankheiten, *Wien. med. Wchnschr.* **64**:1821, 1887, 1914.

18. Weidenfeld, S.: Ueber mechanische Reizbarkeit der Haut (Dermographismus), zugleich eine Studie über Adrenalinwirkung auf die Haut, *Archiv. f. Dermat. u. Syph.* **99**:229-272, 1910.

plaster, although when the inflammation had reached a certain grade the subsequent application of epinephrin did not affect the process.

Since itching is such an important symptom of eczema, it is interesting to review Winkler's¹⁹ work on that subject. We are apt to explain the presence of eczema as the result of itching and subsequent scratching, but, as Kreibich has pointed out, eczema is uncommon as a complication of some of the worst of the itching dermatoses, such as lichen planus, dermatitis herpetiformis and winter pruritus.

Winkler was able to dissociate the sensations of the skin and to show that the sensation of itching was a physiologic perception and distinct from the perception of pain. He showed, too, that the sensation of itching is closely associated with the vasomotor system. He found that the anesthetic zones in hysteria were insensitive to itching, as shown by the absence of the usual rise of blood pressure. Cocain prevented the perception of itching. Skin into which epinephrin had been cataphoretically applied was insensitive to itching, and an itching area could be relieved in the same way. Winkler also showed that an area denuded of epidermis did not itch. He concludes that the perception requires the presence of the intra-epithelial nerve endings.

INFLUENCES TENDING TO SENSITIZE THE SKIN

We are prone to explain a given eczema as the result of chemical or other irritation, blaming anything with which the patient comes in contact, be it ever so mild. Even though the patient may have been exposed to the same agent for years, and in spite of the fact that the skin has the ability to a marked degree to develop an immunity to irritating substances, the patient nevertheless develops a dermatitis. We are apt in these connections to speak of the skin as being sensitized and of eczema as being an anaphylactic phenomenon. If we are to continue to hold these views it behooves us to inquire why the skin should, from time to time, become sensitive to external influences, which at other times and often for years have caused no reaction. The important factor would seem not to be the irritating influences, since they are legion both in kind and degree of irritating power, but rather some factor or factors which change some structure in the skin, so that it is more susceptible to external influences.

It has been shown that the epidermis is not at fault. The blood vessels lie too deep to be reached by the external irritant, so we are compelled to fall back on the nervous system. The intra-epithelial nerve fibrils, situated superficially as they are, could be the structure irritated. Remembering Winkler's work and the part played by these structures

19. Winkler, F.: Studien über das Zustandekommen der Juckempfindung, Arch. f. Dermat. u. Syph. **99**:273-334, 1910.

in the sensation of itching and their close connection with the vasomotor system, we can well understand that irritation of these endings might be followed by itching and by vasomotor changes.

It is not difficult to imagine that the irritability of these nerves could be increased or decreased. As an example of the latter could be mentioned the experiments with hysterical patients, quoted in the foregoing, with cocain, etc. Especially do I wish to call attention to the action of epinephrin in diminishing irritability. If the irritability of these nerves can be diminished, naturally we must conclude that it can also be increased.

At this point I should like to corollate the various experimental and clinical observations detailed.

1. It is conceded that eczema is an inflammatory reaction of the skin.
2. The normal skin of eczema patients is especially sensitive to external irritation, be it mechanical, chemical or thermal.
3. The sensation of itching is inherent in the epidermis, is a prominent symptom of eczema and can be prevented and counteracted by epinephrin.
4. Inflammation of the conjunctiva and skin, usually resulting from the use of strong irritants, can be prevented by paralyzing the reflex arc in various ways, among which is ²⁰ the local or subcutaneous use of epinephrin.
5. Since the vasomotor changes in eczema are so intimately associated with itching, and it has been shown that epinephrin prevents them both and is a normal constituent of the blood, it requires no great imagination to suppose that a deficiency of the active epinephrin in the blood could account for the increased sensitiveness of the skin on the one hand and the itching on the other. Might not the epinephrin act on the cutaneous reflex arc? ²¹
6. The rather frequent association of eczema, low blood pressure and asthma, all conditions counteracted by epinephrin, is suggestive, to say the least.

In the experimental investigation of this theory it remains, then, to ascertain whether in cases of eczema the epinephrin in the blood is diminished or not. Unfortunately, at present this is impossible, the amount normally present being so small that with the known tests it is impossible to show a decrease.

Another possibility, however, suggests itself. Might there not be some toxic substance, or substances, which, entering the blood from

20. The passage seems more comprehensible when "or by" is used in place of "among which is."

21. This question is inserted in the author's handwriting in the manuscript.

time to time would, in spite of a normal epinephrin content, act as an irritant to the vasomotor system and especially to the cutaneous reflex arc or neutralize the normal epinephrin action at this point? The rather intimate association between eczema on the one hand and various metabolic and nervous disturbances on the other hand suggested such a possibility.

THE INFLUENCE OF DIET AND THE GASTRO-INTESTINAL TRACT

Especially susceptible of interpretation from this point of view is Jadassohn's ⁴ third group as described in his work on "Hautkrankheiten bei Stoffwechsel Anomalien." This group includes diseases of those organs which have to do with the reception, preparation, distribution and excretion of food materials. Of these, the one which seemed to present the greatest likelihood of being at fault was the gastro-intestinal tract.

Dermatologists have long recognized the fact that various dermatoses are dependent, to a greater or less degree, on abnormal conditions in the gastro-intestinal tract. Especially is this true of eczema. It is not necessary here to call attention to the frequency with which eczema is accompanied by disturbances in the gastro-intestinal tract. You have all considered the subject and arrived at your own conclusions; and yet, as justifying my own point of view, I would like to call attention to the fact that Spiethoff ²² has shown that gastro-intestinal disturbances were found in the following conditions in the percentages given:

TABLE 1.—PERCENTAGE OF CASES IN VARIOUS CONDITIONS IN WHICH GASTRO-INTESTINAL DISTURBANCES WERE FOUND

Pruritus	70
Urticaria and symptomatic erythema.....	58
Strophulus	82
Rosacea	75
Eczema	54
Infantile eczema	52

In this connection, we believe a consideration of the cutaneous diseases of animals would help us to an adequate realization of the close connection between the gastro-intestinal tract and cutaneous diseases. Whereas eczema forms from 30 to 50 per cent. of all skin diseases in human beings, in animals it is found in about the percentages given in Table 2.

The disease has not been described in wild animals or those in captivity. It seems to be confined to the domestic animals, and among these the carnivora appear to be especially predisposed.

22. Spiethoff: Magendarmstörungen bei Haut- und Schleimhaukerkrankungen, München. med. Wchuschr. 59:991-992, 1912.

With the exception of ergotism, urticaria and pellagra, we can recall no cutaneous disease which is known to be due directly to food. In animals there are a number described, and veterinarians call especial attention to the close association between food intoxication and cutaneous eruptions. It is possible that the diet of animals is so limited that in any deviation followed by a skin disease the association is obvious. Be that as it may, the fact remains that if the limited diet of animals is so important a factor in the production of skin diseases among them, the varied diet of human beings, while making the problem more difficult, also makes it more important.

TABLE 2.—ECZEMA IN ANIMALS

	Percentage of All Skin Diseases
Dogs	7
Cats	4
Birds	3
Horses	0.5
Cattle	Uncommon

I think we shall have to admit that the gastro-intestinal tract has an influence on the skin, far greater than that of any other organ. The writer has been impressed in particular with the frequency with which constipation, high protein diet and alcoholism have occurred in these cases of eczema.

Luithlen has shown that in animals the reaction of the skin to irritants is modified by diet, particularly in that a vegetarian diet diminishes the reaction. Bulkley has frequently called attention to the advantages of such a diet in the treatment of eczema. Recently Lier and Porges²³ have called attention to the frequency with which subacidity and anacidity is found in cases of subacute and chronic eczema. Block⁴ has shown that dogs from which the pancreas has been removed develop an artificial dermatitis much easier than before removal.

THE ACTION AND FORMATION OF HISTAMIN

All these facts, and many more, could be cited tending to prove that the protein of the food is commonly the deleterious part of the diet. This suggestion, taken in connection with the considerations mentioned before regarding the action of epinephrin, would support the possibility that some substance might be formed in the gastro-intestinal tract which, when absorbed, would neutralize or counteract the action of epinephrin at various points in the body.

23. Lier, W., and Porges, O.: *Dermatosen und Anazidität*, Wien, klin. Wchnschr. **26**: 1974-1976, 1913.

In considering this possibility my attention was directed to beta-imidazolethylamin, a toxic amin formed from histidin, the latter being a product of pancreatic digestion. Beta-imidazolethylamin or histamin counteracts (is an antagonist to) epinephrin at almost all points.

Berthelot and Bertrand ²⁴ showed that this substance was produced in the intestine by the *Bacillus aminophilus intestinalis*. Mellanby and Twort ²⁵ isolated from the ilium a strain of colon bacilli, which was able to form it from histidin, and they were able to demonstrate its presence in the wall of the intestine. Mutch ²⁶ has studied the question of the formation of histamin and other poisons in the ileum of constipated subjects. He shows that 14 per cent. of the protein intake can be recovered at the lower end of the ileum in the form of the simple products of digestion. Eyre ²⁷ has examined the bacterial flora of the ileum of sixteen constipated subjects at operation, and in only one case did he fail to find pathogenic organisms. In a series of constipated subjects operated on by Lane, in those with a blood pressure below 110, Mutch found organisms which produced histamin.

Thus it is seen that conditions which would result in an increase of the unutilized protein or in constipation, could result in an increased formation of toxins. Might not this be the reason for Block's finding of an increased susceptibility to dermatitis in depancreatized dogs instead of a lack of the internal secretion of that organ, as he thought?

Since the lower end of the ileum is especially adapted for absorption, it is readily seen that toxic substances formed there can be absorbed and enter the circulation. It is not necessary that the substances so absorbed be themselves deleterious to the skin, for they may act on some other organ in the nature of a stimulant or depressor. Lane ⁴ has shown the effect of intestinal toxins on the thyroid in the production of exophthalmic goiter, and he has also called attention to the pigmentation of the skin due to intestinal toxemia.

24. Berthelot, A., and Bertrand, D. M.: Recherches sur la flore intestinale; isolement d'un microbe capable de produire de la B-imidazolethylamine aux dépens de l'histide, Compt. rend. Acad. d. sc. Par. **154**:1643-1645, 1912. Recherches sur la flore intestinale; sur la production possible de ptomaines en milieu acide, *ibid.* **156**:1027-1030, 1913.

25. Mellanby, E., and Twort, F. W.: On the Presence of B-imidazolethylamine in the Intestinal Wall; with a Method of Isolating a Bacillus from the Alimentary Canal Which Converts Histidine Into This Substance, Jour. Physiol. **45**:53-60, 1912-1913.

26. Mutch, N.: The Formation of B-iminozolyethylamine in the Ileum of Certain Constipated Subjects; With Note on the Urine in Constipation, Quart. J. Med. **7**:427-443, 1913-1914.

27. Eyre: Quoted by Mutch.

EXPERIMENTAL STUDIES: HISTAMIN

With these ideas in mind the writer undertook some investigations to determine the frequency with which histamin is found in cases of eczema. The method used was as follows:

The stools were heated with an excess of 5 per cent. of hydrochloric acid to hydrolize the fats, then filtered while hot, and to the filtrate phosphotungstic acid was added and allowed to stand twenty-four hours. The precipitate formed was collected and washed with 1 per cent. of hydrochloric acid. This was then suspended in water and treated with a saturated solution of barium hydroxid. After filtering, the filtrate was shaken with ether, which dissolves the amins. To this ethereal solution was added 1 c.c. of ether which had been shaken with hydrochloric acid. This changed the amin to the chlorid. The ether was evaporated and the residue was dissolved in 1 c.c. of distilled water.

Unfortunately, on account of the war, the prohibitive cost of phosphotungstic acid compelled us to limit our examination to one stool. When one considers that Eppinger²⁸ advises the use of a total stool for ten days, the fact that we failed to find histamin in so many of our cases is not at all significant. The test used to determine its presence was to scarify lightly an area on the forearm into which the solution was rubbed. If histamin is present in a concentration of as much as 1:1000, a wheal will form within five minutes.²⁸

The author realizes the fact that the intestine is not the only place in which this or other toxins may be found, and he would call attention to the possibility of these substances being formed in any infected focus accompanied by destruction of tissue. The results obtained were:

[The results were never summarized by the author, possibly because of his dissatisfaction with their incompleteness. At one time he expressed to me the feeling that the cutaneous test used for identifying the histamin was not wholly trustworthy since he had noticed an increasing tendency to reaction in his own skin after performing a number of tests on it. From a table among his papers relating to this work it appears that sixteen analyses for histamin were performed. Of these, three were definitely or strongly positive (one, acute eczema; one, psoriasis and one chronic eczema in a child). Two were rated as \pm (one, chronic eczema; one, exfoliative dermatitis), and eleven were negative as follows: erythema multiforme 1, pellagra 1, dermatitis herpetiformis 1, psoriasis 2, acute eczema 1, chronic eczema 3, pityriasis rosea 1, urticaria 1 and urticaria pigmentosa 1. If it is recalled that Harris was obliged to limit himself to a single stool analysis, when the stools for ten days were called for, the results seem more suggestive.—JOHN H. STOKES.]

28. Eppinger, H., and Gutmann, J.; Zur Frage der vom Darm ausgehenden Intoxikationen. *Ztschr. f. klin. Med.* 78:399-412, 1913.

EXPERIMENTS ON INDICAN

The presence or increase of indican in the urine has long been thought to be of significance in various skin diseases, but the mistake has often been made of considering the indoxyl as the offending agent. It is generally admitted that the amount of indican in the urine is a good index of the degree of intestinal toxemia, although the indican itself is innocuous. Therefore, since we were interested in toxins found in, and absorbed from, the intestine, it was thought it might be of advantage to study the question of indican. Since the question of indicanuria in skin diseases had previously been gone into extensively, it was decided to investigate the question of its presence in the blood.

TABLE 3.—INDICAN *

25 cases of eczema, 21 cases examined:
9 were + + +, all chronic cases.
2 were + +.
4 were +.
6 were trace.
6 psoriasis cases: 4, + + +; 2, +.
In one of these cases the diagnosis was doubtful.
2 cases of dermatitis herpetiformis: 1, +; 1, + +, pink.
2 cases of erythema multiforme: 1, + + +; 1, + +.
2 pellagra: 2, + + +.
1 generalized exfoliative dermatitis, trace.
1 pityriasis rosea, trace.
1 diabetes with ecthyma, + +.
1 uremia, + + +.
2 chronic interstitial nephritis, trace.
1 urticaria pigmentosa, + +.
2 urticaria, + + +.
1 angioneurotic edema, +.

* This table is reproduced exactly as it was found in the manuscript.

Obermayer and Popper²⁹ showed it was constantly present in cases of uremia and absent in normal individuals. Tschertkoff³⁰ found that these observers had overestimated its significance, for he found it absent in certain cases of nephritis. He concludes, however, that in normal or sick patients without kidney insufficiency, and irrespective of diet, indican is never found in the blood serum. Patients with marked indicanuria never showed indicanemia. Tschertkoff thinks that the presence of indican in the blood is a more reliable sign of kidney trouble than nitrogen retention.

The indican was extracted from the blood by the method of Obermayer and Popper: Ten c.c. of blood serum were precipitated with 50 c.c. of 95 per cent. alcohol. This was filtered and the filtrate evaporated

29. Obermayer, F., and Popper, H.: Ueber Urämie, Ztschr. f. klin. Med. **72**:332-372, 1911.

30. Tschertkoff, J.: Indikänämie und Urämie (Azötämie), Deutsch. med. Wchnschr. **40**:1713-1715, 1914.

on a water bath. The residue was dissolved in 10 c.c. of water. Two to three minims of a 10 per cent. solution of sugar of lead was added to precipitate the animal³¹ acids. Any excess of lead was precipitated with one minim of a 10 per cent. solution of sodium phosphate. This was filtered and the filtrate contained the indican in 10 c.c. of serum. To determine its presence we made use of a delicate test, originated by Jolles.³² It might be added that this test is not only simple, but is ten times more delicate than Obermayer's. To the filtrate containing the indican was added 1 c.c. of a 5 per cent. alcoholic solution of thymol. To this mixture was added an equal amount of Obermayer's reagent. After standing for fifteen minutes the indican was shaken out with chloroform.

ANTITRYPSIN DETERMINATIONS

One hears so much these days concerning the skin reactions due to the trypsin-antitrypsin balance, that it was thought possible a study of the antitrypsin control of these cases would be interesting. One can imagine that chemical irritants penetrating to the rete mucosum could adsorb antitrypsin, resulting in a solution of the epithelial cells and vesicle formation. The method used was that of Puillet and Morel.³³

TABLE 4.—RESULTS OF EXPERIMENTS WITH ANTITRYPSIN *

Of 12 cases of eczema examined:
8 were below normal
2 were above normal
Of 5 cases of psoriasis examined:
4 were below normal
1 was above normal—gave slight indican
Of 6 control cases of various diseases:
4 were normal or above
2 below normal. One of these was a possible parapsoriasis

* The normal finding is 60.

ABDERHALDEN REACTIONS

While the primary pathologic change in eczema is in the corium, there is secondarily a destruction of epithelial cells of the rete mucosum. Therefore it was thought that a study of the Abderhalden reaction might reveal something of interest. A substrate was prepared of the epidermis of a child 11 days old. At the same time substrates of various organs were used. The results are not at all conclusive, and until we have a satisfactory explanation of this reaction no conclusions can be drawn from them.

31. This is presumably a stenographic error for "amino."

32. Jolles, A.: Ueber eine neue Methode zur quantitativen Bestimmung des Indikans im Harne. *Ztschr. f. physiol. Chem.* **44**:79-103, 1915.

33. Puillet, P., and Morel, L.: L'index antitryptique dans les maladies mentales. *Rev. de psychiat.* **18**:249-259, 1914.

THE ^AROLE OF THE ENDOCRINE GLANDS IN THE ETIOLOGY AND TREATMENT OF ACNE

PRELIMINARY REPORT

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The interrelation of the endocrine glands and the skin makes an apparent manifestation in a condition which the dermatologist is so frequently called on to treat, and which to my mind has not been coped with in an efficient manner, namely, acne.

During adolescence the entire system is affected by the changes which are occasioned by the introduction into its life of an entirely new phase and character. The appearance of acne at the beginning of this unstable cycle of the life of the human being points strongly toward the veracity of my introductory statement that etiologically the basic factor may justly be looked for in a deranged endocrine mechanism, the poise of which suffers severely by the advent of a physiologic and biochemical change caused by the new processes which were ushered in by the active participation of the gonads in body metabolism.

ENDOCRINE IMBALANCE

In the make-up of the fundamental structure of human economy, the endocrine system correlated by the vegetative nervous system plays an important function—that is, balance of metabolism. When any part of this mechanism is called on by the growing body needs or growing organ needs or by pathologic processes or by toxic influences of chemical, mechanical, bacterial or physical nature for altered activity,¹ an imbalance will result. If this derangement takes place gradually, it may be taken care of by a reestablishment or readjustment on the part of the other endocrine glands, but if the imbalance is so rapid that the other endocrine glands are unable to respond in an efficient way, the body will show visible signs of this metabolic imbalance, which has been newly established.

Some such condition arises when puberty is reached and apparent functioning of the gonads makes this change in both the body and the mind of the person as he matures in sex.

1. Reede, E. H.: The Rôle of the Vegetative Nervous System in Diseases of the Skin, *J. Cutan. Dis.* **36**:505 (Nov.) 1918.

It is generally recognized that gonad activity has a distinct bearing on the endocrine system. Endocrine imbalance at the beginning of puberty and at the menopause in woman depends on the inability of the entire endocrine system to adjust itself and to cope with the advent of a new activity in the first instance and the withdrawal of necessary bodily hormones in the latter case. Sudden changes in either way cause the same marked effect as does the slow and long progressing establishment of gonad function. If one adds to this a slight disturbance of another endocrine gland due to some intercurrent or previous infection or other pathologic condition congenital or acquired, readjustment to the new state becomes a more difficult problem for the burdened body and its constituent endocrine mechanism to overcome or to cope with.

There is a visible manifestation of this beginning gonad action in a response to development in certain physical characteristics both in male and female, and the appendages of the skin play an important part under this new regimen as they are awakened from their quiescent stage. This is amply demonstrated by the appearance of pubic and axillary hairs.

A stimulus so powerful as to actuate these hair follicles may have the same stimulating effect on sebaceous and pilosebaceous glands and may be answered by an increased production of their glandular acidity.² Should this new endocrine change be gradual, and should this new stimulus be slow, the ducts of the sebaceous glands can carry off the increased amount of sebaceous secretion, but if time for the adjustment is not given, the ducts cannot conveniently perform their function, and stagnation results.

Suboxygenation of the tissues may be in a great measure the result of the endocrine imbalance, which the body is unable to accommodate. This lack of oxygenation manifests itself in local hyperemia and congestion, which is also an important factor in stagnation and acne formation.

Every one who is concerned in this medical entity speaks of a peculiar type of skin which is necessary for a suitable soil for the development of acne—the oily, seborrheic skin, which oozes sebaceous secretion, with its sluggish and lazy appearance. Dr. Fred M. Jacobs called it “a sad looking skin,” which is a very appropriate and picturesque description. May this not be taken as a physiologic expression of endocrine imbalance, as the dry skin and hair, the pads of subcutaneous fat are necessary to complete the syndrome of hypothyroidism?

That these overloaded sebaceous glands, periglandular structures and ducts are an easy prey for organisms occurring on the skin can be

2. Sutton, R. E.: *Diseases of the Skin*, St. Louis, The C. V. Mosby Co., 1919, p. 883.

readily perceived, but that this is only a secondary and not the primary point of the pathologic process is a point of great therapeutic importance.

Stagnation in the excretory ducts of the testes and ovaries from lack of physiologic use may also be a determining factor in this endocrine imbalance. I have four cases of acne, all in males, who had distressing vesical symptoms to such a degree that they warranted the seeking of advice from a genito-urinary specialist. In each case an overdistention of the seminal vesicles was found, which on slight massaging evacuated a large abundance of fluid.

I have collected cases of acne in persons between the ages of 30 and 42 years. Each case may be classed in the "unmarried" or, in two instances, in the "widow" social status of more than ten years' standing. What inference may be made from this? Is it merely a coincidence, or is the observation of the late Joseph Zeisler correct, that when normal sexual relation is established, as in the marital state, acne disappears? Or is the mere pelvic irritation which the stagnation causes sufficient, without the involvement of the endocrine system, to produce a hyperstimulation of the sebaceous and pilosebaceous glands to abnormal activity?

To accept the view of endocrine imbalance, that as the patient reaches maturity it tends to adjust itself along physiologic lines, may also explain the self limited character of acne; and the establishment of this balance may be greatly aided by "the establishment of normal sexual relations," of which Joseph Zeisler speaks.

If we accept the acne bacillus as the exciting agent, the removal of the necessary soil for its development will determine its extinction and not the development of any particular type of resistance by the body to overcome the invasion and activity of this organism. I think nature points definitely to treatment of the endocrine mechanism in order to help out this system.

TWO TYPES OF PATIENTS WITH ACNE

The clue to the situation may be obtained from the behavior of general body metabolism. Early in the history of dermatology two distinct types of patients presenting acne were described—the thin emaciated, anemic type and the stouter, full blooded or plethoric type. In each instant there is an endocrine imbalance.

The first type falls into the group of patients who present the well established syndrome of thyroid toxicosis with increase in metabolism as a whole, the rapid burning up of tissues unable to overcome or resist infections and intoxications. This does not mean, however, that certain localized areas of the body may not be suffering from under-oxygenation, such as may occur in the sebaceous glands or in any of

the skin appendages. The second type is the sluggish person in whom there may be, and in whom there usually is, lessened metabolic activity, such as may be demonstrated by basal metabolic study. In these a lessened localized oxygenation is consistent with the lessened general metabolic activities.

Taking for a basis body metabolism, I have classified patients with acne into two classes:

1. Those presenting increase in metabolic activities—thin, anemic, undernourished patients whose thyroid gland activity is increased in a compensatory measure to cope with the endocrine imbalance produced by the gonad activity, practically thyroid toxicosis.

2. The opposite type—lazy, plethoric, overnourished, closely bordering on lowered thyroid gland activity.

TYPE 1: In addition to regulating the patient's habits, enforcing dietetic and hygienic measures, scrupulous cleansing of the skin with hot fomentations at night and frequent washings during the day, aseptic removal of comedones and opening pustules, the patient is given suprarenal gland substance, 5 grains, three times a day at 8 a. m. and at 2 and at 8 p. m. for two weeks. At the end of this time if no symptoms to the contrary should arise, the dose is given four times a day at 8 a. m., at 12 and at 4 and 8 p. m., and is usually not increased.

This treatment is continued for a period of two months, at the end of which time it is discontinued or kept up, as may be necessary, depending on the patient's physical condition, which usually improves considerably, including the appearance of the acne.

TYPE 2: The patient is instructed to carry out the foregoing measures, except as regards endocrine medication. In these cases I administer thyroid gland substance, $\frac{1}{4}$ of a grain, three times a day, and instruct him to observe his pulse just before arising and also ten minutes after retiring. The record of these observations is brought in to me in one week. If the pulse remains stationary, the dose of thyroid extract is increased cautiously and its administration is continued for two months or longer, depending on the patient's condition or presentation of untoward symptoms.

This addition of the thyroid substance answers a double purpose. First, it relieves the laboring gland which is trying hard to equalize the normal endocrine balance, and thereby permits this organ to take on its normal function after a shorter or longer period of time depending on the amount of impairment which may exist.

Second, it not only helps in the burning up of tissues, but increases the capacity of the thyroid gland to carry out its other functions which, according to Sajous,³ is the protection of the body against infections and

intoxications and, as McCready³ puts it, "The use of the thyroid gland is indicated when metabolism is retarded from any cause and to combat infectious processes.

COMMENTS

I am aware of the preliminary nature of this paper and of the possible faulty presentation of my conception, but I am daily impressed with the correctness of the conception that the underlying etiologic factor in acne is somewhere in the domain of the endocrine glands—probably in the gonads. In a good many instances the endocrine administration described in the foregoing is supplemented with ovarian or testicular extract administration, but this I refrain from as much as I can in order to facilitate observation of these cases without polypharmacy, which may be confusing.

The administration of dry gonad extracts has proved unsuccessful in my early efforts, and results cannot compare with the therapy described.

7133 Jenkins Arcade.

3. McCready, E. B.: *Organotherapy in Certain Diseases and Conditions of Childhood*, *Med. Rec.* **96**:529 (Sept. 27) 1919.

CONCERNING THE SPECIFICITY OF CHOLESTER- INIZED ANTIGENS IN THE SEROLOGIC DIAGNOSIS OF SYPHILIS *

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In spite of extensive and intensive studies which have been made of the Wassermann reaction since its introduction in 1906—or perhaps, because of them—the test might almost be said, at the present time, to be undergoing its “trial by ordeal.”

It is to be regretted that much of the criticism of the reaction as concerned with its specificity and reliability has come from clinicians not always, perhaps, fully qualified to express a dogmatic opinion, and in this connection it must be noted that the mere possession of expert and skilled knowledge of genito-urinary diagnosis and treatment does not always predicate an equally expert and skilled familiarity with the finer details of complement-fixation technic, particularly with regard to the numerous important factors which may be responsible for variations in reports and results.

It seems obvious that it is the duty of the clinician to acquaint himself with the details of complement-fixation technic to such a degree as will enable him to interpret properly the reports received.

Errors there have been, it is true, and for many the true responsibility may be laid to the lack of a standardized technic by which reactions might be made strictly comparable. Contradictory reports on the same blood, variations in the strength of the reaction as reported by different observers, and—what is of vital importance—the lack of any standard by which to distinguish the competent serologist, have all been contributory factors and, in part, responsible for the feeling among many clinicians that a perceptible number of Wassermann reports are of little value.

Of almost equal importance with the necessity for a standardized technic is the necessity for a standard method of reporting the results of the test. It is impossible to compare or evaluate reports which read simply “positive” or “negative” even when qualified as to the degree of fixation. As has been stated elsewhere,¹ a Wassermann report should

* From the Laboratories of the Pittsburgh Hospital.

1. Kilduffe, R. A.: The Practical Value and Utilization of the Wassermann Test in General Practice, *Arch. of Diagnosis* **12**:25, 1920.

consist of a statement in detail as to the antigens used, the reaction to each, and the interpretation of the reaction as a whole; and it is debatable whether or not the serum dosage should not be included and the method of fixation—ice chest or water bath.

Such a method of reporting would avoid the occurrence of "positive" and "negative" reports on the same serum when tested by different laboratories for, if it is known that one laboratory is using a liver extract only, while the other uses an additional cholesterinized extract, the apparent lack of agreement between the reports disappears, and the two reports are easily compared.

As noted in a previous communication, the writer uses a triple antigen battery and reports: Cholesterinized extract of the human heart ++++, acetone-insoluble lipoids of the human heart ++++, alcoholic extract of a syphilitic liver ++++, interpretation, very strongly positive.

Regarding the interpretation, trite though it may be, it seems worth while again to emphasize what has been emphasized before,² that the clinical value of any laboratory procedure lies, not in the test but in its interpretation, and that this not infrequently necessitates a correlation of the test with the patient and the clinical conditions.

It is generally recognized that the Wassermann reaction is not a true biologic reaction but a chemical reaction closely related to, and concerned with, lipoidal and colloidal substances. Properly performed with adequate controls and, above all, properly interpreted, its specificity is relatively absolute and the reaction can be depended on. As expressed by Pollitzer,³ "a strongly positive Wassermann reaction is found only in syphilis, and a strongly positive Wassermann reaction means syphilis (barring leprosy and yaws)."

Probably one of the most important advances in the technic was the introduction by Sachs of cholesterinized extracts as antigens, the delicacy of which is universally admitted. Concerning their specificity, however, there has been much discussion, and this question becomes of importance as concerned with the proper interpretation of the reaction when we are confronted—as all serologists using cholesterinized antigens have been—with a serum from a patient perhaps clinically free from all signs of syphilis, with a negative history, but who, nevertheless, gives a strong fixation with the cholesterinized extract, while the acetone and liver extracts remain negative.

2. Footnote 1. Variations in the Wassermann Reaction: A Reply, *J. Lab. & Clin. Med.* **6**:98 (Oct.) 1920. *Urinalysis and the General Practitioner*, Arch. Diagnosis, October, 1915.

3. Pollitzer, S.: General Prognosis of Syphilis in the Light of Recent Progress, *J. A. M. A.* **74**:775, 1920.

While the true significance of this phenomenon, in the case of a treated patient, or one under treatment, is looked on as indicating the necessity for further treatment and as indicating a residuum of syphilitic "reagin" in the blood, the same opinion is not universal when concerned with a serum tested for diagnosis under the conditions noted in the foregoing.

Because of the comparative frequency of this type of reaction it has been thought of interest, and possibly of value, to gather the opinions of various observers on this point and to compare the results of tests with various antigens as far as possible with the true conditions as indicated by the after clinical course or revised history of the case.

Because of the fact that the earlier reports following the introduction of cholesterinized antigens were unanimous in interpreting such reactions as due to proteotropic fixation and in regarding them as non-specific, and because most of the work leading to their true valuation has been of comparatively recent origin, references from the older literature are not quoted nor has an endeavor been made to obtain a complete and exhaustive bibliography. If, as a result of this communication, a generalized expression of opinion is excited or obtained, its purpose will have been fulfilled.

If, as held by a few serologists, the Wassermann reaction is a true, biologically specific, test indicating an interaction between a specific antibody and its specific antigen, the only true biologic antigen possible would be an aqueous extract of *Spirochaeta pallida*; but experience has shown such antigens to be relatively useless. The use of alcoholic extracts of syphilitic fetal livers originated with the idea of retaining a biologic specificity, despite the fact that the coincident presence of liver tissue extractives introduced a nonspecific factor. While such antigens are extremely useful and reliable, it should be recognized and emphasized that the mere presence of spirochetes does not necessarily indicate that an extract made of such a tissue will be a good antigen; in fact, the antigenic property may be almost nil.

A few observers, however, holding the reaction to be a biologic one, proclaim such extracts to be "the only proper antigens with the highest degree of accuracy," admitting, however, that alcoholic extracts of normal organs and tissues containing lipoids are "useful and accurate to a degree."⁴

The fact that positive complement-fixation tests may be obtained, regardless of the antigens used (cholesterinized heart extracts, acetone-insoluble lipoids, and alcoholic syphilitic liver extracts), with the serums of rabbits and other animals definitely known to be free from syphilis, is conclusive evidence of the absence of biologic specificity in the test

4. Laird, J. P.: Bull. 104, Penn. Dept. of Health, p. 171.

as at present performed. The objection to the use of cholesterinized extracts on the score of nonspecific fixation applies, therefore, in the face of these facts, to the other antigens as well.

It is certain that the lipoids contained in a cholesterinized antigen are capable of inter-reacting with the syphilitic "reagin," but whether or not they may bind complement in its absence when used in amounts far below their anticomplementary dose is the question at issue. With few exceptions,⁵ serologists are in accord as to the advisability of including a cholesterinized antigen in all tests. The degree to which the cholesterinization is carried, however, and the method by which it is produced, vary. While a large number of serologists use a fully saturated solution. (from 0.4 to 0.7 per cent.), some produce saturation at room temperature, others at 37.5 C., and still others in the ice chest. Not infrequently a half-saturated extract is utilized which, in my experience, has proved of equal value with one fully saturated.

LITERATURE ON THE SUBJECT

While, as a rule, the cholesterin is added to the extract as the final step in its preparation, English workers largely follow the method of McIntosh and Fildes⁶ who add to the alcoholic heart extract at the time of use 1 per cent. of alcoholic solution of cholesterin in the proportion of three parts of the former to two of the latter, further diluting immediately with normal salt solution. In my experience this method produces an antigen of remarkably uniform antigenic and anticomplementary dosage.

Walker and Swift⁷ were among the earliest to recommend the continuation of treatment until tests are repeatedly negative with cholesterinized extracts, an opinion now generally accepted.

Webster⁸ expresses the opinion that "Noguchi's antigen (acetone-insoluble lipoids) and Sach's alcoholic heart antigen with cholesterin are by far the most reliable and constant ones thus far introduced." He believes, however,⁹ that "cholesterinized extracts may yield nonspecific fixation in a certain number of cases, but its *greater sensitiveness*"¹⁰

5. Laird (Footnote 4) holds that cholesterinized antigens are not only less useful than liver extracts, but also distinctly dangerous as giving from 10 to 20 per cent. false positives.

6. McIntosh, J., and Fildes, P. G.: The Wassermann Test. Med. Res. Comm., Special Report, Series 14, Standardization of Path. Meth., March, 1918, p. 32.

7. Walker and Swift: J. Exper. Med. **18**:75. 1913.

8. Webster, R.: Diagnostic Methods, Ed. 6, Philadelphia, P. Blakiston's Son & Co., p. 683.

9. Footnote 8, p. 685.

10. Italics are author's.

enables it to catch a certain number of positives that are doubtful with other antigens"; he further adds that "this antigen may be recommended as a standard one and should be included in every test even though a number of antigens be used with it." The criteria, whereby it is looked on as indicating true fixations with other antigens, doubtful but false fixations when acting alone, are not indicated.

Kolmer¹¹ recognizes cholesterinized heart extracts as "highly sensitive antigens" which occasionally give "*faint*¹⁰ positive reactions with negative serums." He calls attention to the fact that they often react strongly when other antigens are negative in long-standing cases thus indicating the necessity for further treatment, so that "they have their greatest value as a guide to treatment." While believing that "there is no better guide to the state of infection than repeated negative tests with a cholesterinized antigen," he also believes that they should not be used alone in diagnosis.

A significant statement is that "we have practically never found a serum that was negative to cholesterinized extract and positive to a luetic liver extract." I have observed occasional instances of this in the past few years.

According to Kolmer, in primary syphilis, using cholesterinized heart extracts, reactions may be secured earlier and in a larger percentage of cases, a finding to which the writer's experience can testify.

The same observer,¹² in another place, says: "Cholesterinized antigens have proved, in my experience, quite delicate, reliable, and highly satisfactory in the Wassermann reaction *using heated serum*, but with active serum . . . are prone to yield falsely positive results." In the same paper he says that "in comparing the Wassermann with other tests, a serum was considered positive if the reaction with cholesterinized human heart extract was positive even though the reaction with acetone insoluble lipoids and alcoholic luetic liver was negative, as *I have learned from experience to place reliance upon results obtained with a properly prepared and titrated cholesterinized extract.*"¹⁰

Larkin and Cornwall,¹³ in reporting the results of examinations made on 319 spinal fluids obtained from cases of neurosyphilis, emphasize the fact that "without the employment of an antigen reinforced with cholesterol the complement-binding power of the spinal fluid will be undetected in 12% of cases." The tabulated series of these examinations shows that the cholesterinized antigen gave 61.1 per cent. of posi-

11. Kolmer, J. A.: *Infection, Immunity and Specific Therapy*, Ed. 2, Philadelphia, W. B. Saunders Company, p. 445.

12. Kolmer, J. A.: *The Serum Diagnosis of Syphilis and Gonorrhea Employing Human Complement*, Am. J. Syphilis **2**:739 (Oct.) 1918.

13. Larkin, J. H., and Cornwall, L. H.: *The Value of Laboratory Diagnosis in Neurosyphilis*, Am. J. Syphilis **3**:76 (Jan.) 1919.

tive reactions while the plain alcoholic extract gave 49 per cent., and it is of special interest and significance that these positive results were all supported by corroboratory clinical and other laboratory findings.

Roderick,¹⁴ reporting the results of Wassermann reactions with cholesterinized human heart and acetone-insoluble lipoid antigens in a series of 5,787 tests, found that the antigens disagreed in 39 cases, of which 35 had a definite history of syphilis from one to thirty-seven years previous to the test; 2 were probably syphilitic; 1 doubtful; and one occurred in a patient from India who gave a history negative for syphilis but positive for malaria.

In thirty-three of thirty-five of these cases the acetone antigen was completely negative; in one of the remaining two it was + and in the other ++. He calls attention to the fact that these tests were made for diagnosis and emphasizes the fact that, if the cholesterinized heart extract had not been used, "thirty-three of the thirty-nine patients would have been given a clean bill of health, whereas the cholesterin-reinforced product was able to detect the presence of syphilitic antibodies and treatment was instituted." The paper also contains the statement that "in some cases where syphilis is not present a *slight* ¹⁹ degree of inhibition—10 per cent. or less—will sometimes occur."

Graves,¹⁵ referring to the Wassermann tests performed on cadaver serums, one of the antigens being a cholesterinized extract (which, in the latter part of the series, constituted the sole antigen), says: "Cholesterinized antigens did not give false reactions as far as could be ascertained from the clinical data," but emphasizes the fact that he requires at least a ++ reaction for a diagnosis.

Owen,¹⁶ while holding that cholesterinized heart extracts give "a certain percentage of false reactions," in 2,241 reactions had 1.5 per cent. of cholesterinized positive reactions all of which were in old, treated cases, some going as long as 15-20 years without treatment."

Of particular significance are the findings of Ebersson and Engman ¹⁷ reporting a study of seventy-five asymptomatic, latent syphilitic patients, serologically cured (blood and spinal fluid Wassermann reactions were negative), who demonstrated by animal inoculation the presence of living spirochetes in five cases, four of which gave positive reactions with cholesterin antigens only.

14. Roderick, C. E.: Cholesterin Alcohol Extract of the Human Heart as an Antigen in Complement-Fixation Tests for Syphilis, *Am. J. Syphilis* **3**:248 (April) 1919.

15. Graves, Stuart: The Value of Postmortem Wassermann Reactions, *J. A. M. A.* **75**:592 (Aug. 28) 1920.

16. Owen, R. G.: Discussion of Graves' paper.

17. Ebersson, F., and Engman, M. F.: An Experimental Study of the Latent Syphilitic as a Carrier, *J. A. M. A.* **76**:160.

Even this more or less cursory review is sufficient to establish these facts: (*a*) Cholesterinized antigens are exceedingly delicate; (*b*) they should be included in every test; (*c*) they are of great value in following the course of treatment; (*d*) they will, when properly used, detect cases of syphilis not picked up by other antigens in common use.

RELIABILITY OF CHOLESTERINIZED ANTIGENS

As to their reliability, we find serologists in one breath extolling them and in the next deprecating their specificity.

Given a serum from a patient with a chancre of ten days' to two weeks' duration, a reaction may frequently be obtained with a cholesterinized extract ranging from + to +++++, which there is no hesitancy in reporting as a true positive. What is to be the interpretation of this reaction when the knowledge of the presence of the chancre is not at hand? If it is a true positive in the one case, may it not be equally so in the other? Obviously, the reaction is properly interpreted in the light of its correlation with the patient, which, unfortunately, is not always possible in the laboratory.

If, in the absence of any explanatory or corroborative data we are to look on cholesterin + reactions as dubious, it is obvious that the Wassermann reaction should not be performed with these as the sole antigens, an opinion in which numerous observers concur.

In spite of this, however, the antigen supplied to the laboratories of the A. E. F.¹⁸ was a cholesterinized extract of beef heart (half-saturated), no other antigen being used, and on the results of these reactions the diagnosis of syphilis was unhesitatingly made and entered on the soldier's record. The latest edition of the Laboratory Manual No. 6 U. S. Army does not mention the antigen to be used except to say that it is supplied by central laboratories.

All of the so-called "standard methods" recommended for use in the British Expeditionary Force¹⁹ made use of cholesterinized antigens only, being those of Harrison,²⁰ Browning²¹ and McIntosh and Fildes.²²

18. Personal knowledge.

19. The Wassermann Test, Brit. Med. Res. Comm., Special Rept., Series 14, Standardization of Path. Meth., Nov. 1, 1918.

20. Harrison, L. W.: Method of Rochester Row Military Hospital, Brit. Med. Res. Comm., Special Rept., Series 14, Standardization of Path. Meth., p. 13.

21. Browning, C. H.: Middlesex Hospital, Brit. Med. Res. Comm., Special Rept., Series 14, Standardization of Path. Meth., p. 27.

22. McIntosh, J., and Fildes, P. G.: Royal Naval Hosp. and London Hosp., Brit. Med. Res. Comm., Special Rept., Series 14, Standardization of Path. Meth., p. 32.

In a recent paper, Hinton,²³ detailing a technic widely adopted throughout Massachusetts and used in such institutions as The Boston City Hospital, Massachusetts General Hospital, Peter Bent Brigham Hospital, Boston Board of Health, etc., gives an antigen battery consisting of three antigens: two different cholesterinized extracts of human heart, and one cholesterinized extract of guinea-pig heart.

These workers are willing to hazard a diagnosis of syphilis on the results of tests with cholesterinized extracts alone even though it is inevitable that some of their serums must be serums which would be negative with acetone extracts and syphilitic liver extracts, were they also used, and although some of their tests must be "weakly positive."

TECHNIC USED BY AUTHOR AND RESULTS OBTAINED

According to the teachings of Kolmer, I believe that at least a triple antigen battery should be used, consisting preferably of cholesterinized extract of human heart, acetone insoluble lipoids of human heart and a plain alcoholic extract of syphilitic fetal liver. I would lay great emphasis on the careful titration of all antigens for both antigenic and anti-complementary doses and would insist that no antigen should be used whose antigenic dose is greater than one-fifth of the anticomplementary dose, and that the antigens should be paralleled with others of known value in not less than one hundred tests before being placed in use. They should be retitrated at least once a month. Using such a triple antigen battery, it is readily demonstrated that, under treatment, the first reaction to disappear is that with the alcoholic extract of syphilitic liver, the next that with the acetone-insoluble lipoids, and the last the reaction with the cholesterinized extract.

Using such a technic, in the last 1,000 Wassermann reactions in these laboratories reactions to cholesterinized extracts alone were obtained in the following degree: Plus 4 reactions, thirty-one or 3.1 per cent. The majority of these specimens were obtained under circumstances which precluded obtaining a history. In one case there was a history of syphilis two years before with treatment consisting of eighteen neo-arsphenamin injections and mercury in addition. Plus 3 reactions, three. One patient had the initial lesion ten days before the test; one had had a chancre twenty years previously; and no history was obtained in the third. Plus 2 reactions, two. One of these patients had had a chancre and had received five injections of neo-arsphenamin. Plus 1 reactions, eight. No history obtained in any case.

From personal experience and the data presented, the writer would look on a ++++ or +++ reaction to a cholesterinized extract alone

23. Hinton, W. A.: A Standardized Method for Performing the Wassermann Reaction. *Am. J. Syphilis* 4:598 (Oct.) 1920.

as indicating syphilitic infection, and on any reaction below ++ as decidedly suspicious and as indicating the necessity for a further investigation, unless the specimen was taken during a febrile period it should be remembered that the reaction must be interpreted in close correlation with the individual patient.

The absence of a history or of clinical signs in a cholesterin ++++ case should not be allowed to overrule or cast doubt on the reaction, for the history is too often unreliable and the absence of clinical signs too often misleading.

SUMMARY

A partial résumé of recent literature concerning the specificity of cholesterinized antigens is presented and the incidence of cholesterin postive serums in a series of 1,000 Wassermann reactions is reported, together with certain conclusions drawn therefrom.

CONCLUSIONS

1. All Wassermann reactions should include at least three antigens of varying delicacy: preferably a cholesterinized extract of human heart, an extract of acetone-insoluble lipoids, and an alcoholic extract of syphilitic fetal liver.

2. Wassermann reports should give the antigens used, the reaction to each, and the interpretation of the reaction as a whole, with, perhaps, the dose of serum tested and the method of fixation.

3. Reactions with cholesterinized antigens of ++++ or +++ degree are indicative of the presence of syphilitic "reagin" in the blood.

4. Reactions with cholesterinized antigens below the grade of +++ should be looked on as suspicious and as indicating the necessity for further investigations and should not be looked on as invariably false or proteotropic fixations.

5. Syphilitic patients under treatment should remain under observation until complement-fixation tests are repeatedly negative to cholesterinized extracts, not only with the blood serum but, if possible, with the spinal fluid.

ADDENDA

Since this paper was written a notice of work done by Wassermann²⁴ is available concerning the results of investigations begun before the war and only recently completed. It is said that he has demonstrated in the blood of syphilitic patients a lipid which has been isolated, and that he has shown that this substance is capable of causing the production of true antibodies. To quote from the report: "The syphilitic suffers from

24. Berlin Correspondence, J. A. M. A. **76**:463 (Feb. 12) 1921.

an inversion (*Umstellung*) of lipid metabolism which explains why the Wassermann reaction is positive, not only with extracts from the organs of syphilitic children, but also with all organ extracts containing lipid-like substances."

Details as to the character of his experiments are not as yet available, but it can be assumed that these results will give further assurance as to the specificity of cholesterinized extracts as antigens in the Wassermann reaction.

Hinton,²⁵ in a recently published study of the specificity of cholesterinized extracts based on 4,565 cases, concludes them to be of high specific value and says that "the percentage of false positive Wassermann reactions must be very small when carefully tested cholesterinized antigens are used," and holds that "they have a high specific inhibitory value and are superior to the plain extracts or artificially prepared lipoids."

There seems little doubt but that a careful and exhaustive study of recent literature would show that these views are gradually gaining a wider and more general acceptance.

25. Hinton, W. A.: Specific Inhibitory Action of Cholesterinized Antigens in the Wassermann Test, *Am. J. Syphilis* **5**:1, 1921.

MULTIPLE LYMPHANGIOMATOUS TUMORS OF THE SKIN *

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CHICAGO

The subject of lymphangioma has been carefully investigated, and many excellent papers on the subject have been written. Conspicuous among these have been the works of Torok and Noyes,¹ Wegner, Francis,² Leslie Roberts,³ Nasse, Van Harlingen,⁴ Gottheil,⁵ Fox, Pospelow,⁶ and Heidingsfeld.⁷ The paucity of literature on the subject of lymphangioma of the type this paper describes prompts me to report a case which is unique in many respects.

REPORT OF A CASE

History.—G. L., a Greek, 48 years of age, was referred to the dermatological department of the Central Free Dispensary on May 4, 1920, by Dr. Y. N. Levinson. He complained of pain in his abdomen, dizziness and a cutaneous eruption on his hands, forearms and foot. His temperature was 98.6, pulse rate 96, and respirations 18. He was a well developed man, 5 feet, 8 inches in height and weighed 147 pounds. He was married and had two healthy children. He had always enjoyed fair health. He had had gonorrhea eight years ago; he denied syphilis, but his Wassermann reaction was + + +. Three years ago he was burned by molten iron splashing on the back of his left hand. He ascribed the eruption which had been present for the past two years to that accident.

This cutaneous eruption was somewhat pruritic, but his principal complaint was pain in his abdomen. This had been present for only three weeks. It was aggravated by constipation, and when his bowels operated regularly he felt much better.

Examination.—A general medical examination disclosed no organic trouble. A slight leukocytosis was present, and his Wassermann reaction was positive.

*From the Department of Dermatology and Syphilology, Rush Medical College.

1. Noyes and Torok: Brit. J. Dermat. **2**:359, 1890, and **3**:8, 1891.

2. Francis: Lymphangioma Circumscriptum, Brit. J. Dermat. February, 1893, pp. 33 and 65.

3. Roberts, Leslie: Five Cases of Lymphangioma, Brit. J. Dermat. **8**:309, 1896.

4. Van Harlingen: Transactions of American Dermatological Association, 1881, p. 28.

5. Gottheil: Pseudo-Xanthomatous Lymphangioma, J. Cutan. Dis. **27**:277, 1909.

6. Pospelow: Vrtljschr. f. Dermat. u. Syph. **6**:521, 1879.

7. Heidingsfeld: J. Cutan. Dis. **26**:18, 1908.

The Skin: The patient presented a peculiar cutaneous eruption limited to the dorsal surfaces of both hands, the flexor surface of one wrist and both forearms and the dorsal surface of the third toe on the right foot. Both hands seemed puffy and slightly edematous. They were a dusky, almost bluish red. On the flexor surface of the left wrist was a distinctly elevated lipoma-like tumor with a rounded top, a little larger than a silver quarter. It was bluish red, and on pressure it gave the same sensation of resiliency one feels when pressing an umbilical hernia in an infant. The tumor wall sank in and returned slowly. The cutaneous covering seemed thicker and harsher than normal skin. A larger lesion, the size of a silver dollar, bluish red in color, but somewhat more flabby, was present on the dorsal surface of the left wrist. This lesion was not quite as well defined as was the one on the flexor surface.



Fig. 1.—Lymphangiomatous tumors on dorsum of left hand and wrist of author's patient.

The dorsal surface of the left hand and proximal phalanges of the fingers were covered with about eighteen or twenty lipoma-like swellings varying in size from that of a split pea to that of a hickory nut. They were bluish red, soft and compressible to the touch. The dorsal surface of the right hand was covered with similar lesions though not to as great an extent as the left.

There were on both forearms a chain of rather hard, shotty tumors varying in size from that of a split pea to that of a cherry. The skin covering them was normal in color, and, while they were visible to the naked eye, they were not markedly elevated. On attempting to excise them, they were found to be cystic.

The feet were free from lesions except for one pea-sized lesion on the dorsal surface of the third toe of the right foot.

The large lesion on the flexor surface of the left wrist was punctured with a sterile glass pipet, and a clear amber colored fluid was withdrawn. Probing about with the pipet, this lesion was found to be made up of a number of

multilocular cysts. The roof wall was thick and fibrous. A piece of tissue was excised from this wall, fixed in 10 per cent. formaldehyd solution and stained with various tissue stains.

Microscopic Examination.—The epidermis was considerably atrophied throughout. This was especially noticeable in the stratum mucosum. The stratum corneum, however, was appreciably hypertrophied, and in places seemed to be one-half again the width of the entire epidermis. In places it was distinctly separated from the granular layer by clear cystlike spaces. The stratum granulosum in places was atrophied, only one or two layers of cells being present. It also contained, in several locations, definite cysts lined with cells of its own layer. The nuclei of the cells of the stratum mucosum appeared to be atrophied and surrounded by large vacuolated spaces. A few dividing cells were seen and the papillae were short and blunt.



Fig. 2.—Tumor on wrist with chain of lesions extending up the forearm.

Corium: The upper portion of this layer was made up of a dense band of closely packed connective tissue cells. It was compact and extending down from it into the deeper portions were finger-like prolongations of the same connective tissue. Just below this band were seen numerous small spaces, evidently lymph capillaries, forming a veritable network surrounded by connective tissue cells. In some regions they were so closely packed as to have the appearance of small slits in this connective tissue framework. As one penetrated deeper into the corium, the spaces were larger and more cyst-like. The deepest layers were entirely made up of large and small cysts. These cysts were lined with flat endothelial cells with a round nucleus. They appeared to lie directly on the surrounding connective tissue. In some of these cysts

were seen small collections of red blood cells, in some broken down septums and débris.

The stroma of the tumor was made up of closely packed oval and spindle-shaped connective tissue cells. There were numerous small blood capillaries here and there throughout, especially in the upper layers, together with many small areas of hemorrhage. The elastic tissue was practically absent, and few of the glandular elements were seen. The tumor had none of the characteristics of a malignant one.

Treatment.—Whether or not the patient's syphilis was a definite factor in the production of the tumors is not known. Treatment of the tumors with radiotherapy was begun, and antisyphilitic treatment instituted, but the patient disappeared from observation shortly after.



Fig. 3.—Lesion on dorsum of third toe.

CLASSIFICATION OF LYMPHANGIOMATOUS TUMORS

Unna⁸ divides lymphangioma into three classes: (1) Lymphangioma of the papillary body, which appears in two well characterized forms, the isolated pure lymphangioma superficiale and that superficial form which has a vesicular appearance and is associated with the deep lying lymphangioma. (2) Lymphangioma of the hypoderm, which includes the type described by Pospelow as lymphangioma tuberosum multiplex and another group formed by the solitary lymphangiomatous tumors of the neck and the upper region of the chest so often noted by the

8. Unna: *The Histopathology of Diseases of the Skin*, trans. by N. Walker, New York, Macmillan Co., 1896.

surgeon. (3) Lymphangioma of the subcutaneous vessels. This type is mainly congenital. This anatomic division accords with the clinical conditions since it corresponds to the three different characteristic forms, the lymph vesicles, the lipomatous-like lymph tumors and the so-called lymphangiectases.

According to this classification, the tumors in my case fall into the group classed as lymphangioma of the hypoderm. In a careful search through the literature I find that this case resembles those cases described by Van Harlingen and Pospelow more than it does any other.



Fig. 4.—Atrophied epidermis; lymph capillaries in corium with surrounding cellular infiltration with cysts in lower portion.

CASES REPORTED IN LITERATURE

Van Harlingen's case was that of a girl aged 23 years. There were large numbers of tumors of various shapes and sizes scattered over her entire body. These tumors in some instances resembled flabby molluscum fibrosum growths. In other instances there were smooth, lilac or bluish elevations of the skin varying in size from that of a pinhead to that of a hazelnut. They were all compressible under the finger and gave a sensation when felt like bladders filled

with air. Numerous telangiectatic spots and irregular brownish patches were also present. Histologic examination showed the tumor to be composed of fibrous and granulation tissue with irregular spaces and sections of dilated lymphatic vessels.

Pospelow's case was not purely hypodermal, but Unna feels that it is more characteristic of that class than of any other. It was reported as lymphangioma tuberosum multiplex. The patient was a young girl. There were papillomatous tumors on the genitals, together with other tumors distributed over the entire surface of the body

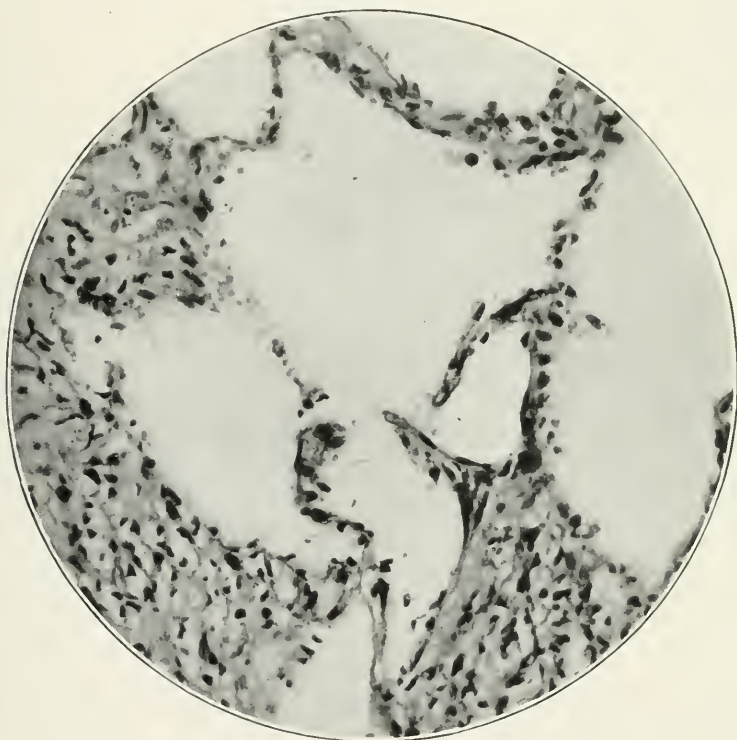


Fig. 5.—Cysts of deeper portions of corium lined with endothelial cells; lymph capillaries and surrounding cellular infiltration.

except the palms, soles and scalp. The largest tumor was a congenital one and was located at the junction of the skin of the chest and mamma. It was the size of a pigeon's egg, and was composed of a number of smaller tumors. The smaller growths varied in size from that of a hazelnut to that of a grape seed. They were soft and compressible and gave the sensation when pressed one experiences on pressing an umbilical hernia in an infant. Microscopically, there were many oddly formed cavities, the largest in the hypoderm, the smallest

in the cutis. They were lined with endothelial cells and contained a quantity of lymph corpuscles. The stroma of the tumors was loose and beset with many small tubes and fissures.

Unna believes that every lymphangiectasis requires for its production a double resistance to the venous and lymphatic circulation and every lymphangioma an abnormal power of proliferation of the endothelium and perithelium.⁹

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9. In addition to the references already given, the following may be of interest:

Ewing: *Neoplastic Diseases*, Philadelphia, W. B. Saunders Company, 1919, p. 228.

Fox: Tiebury & Fox, Colcott: *London Pathol. Soc. Trans.* **30**:470, 1879.

Nasse: *On Lymphangioma*, *Chir. Arbeiten aus Bergmann's Klinik* **14**:1, 1890.

Wegner: *On Lymphangioma*, *Arch. f. klin. Chir.* (Langenbeck's Archiv.) **20**:641.

CHANCRE OF THE GUM WITH REPORT OF A CASE

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Chancre of the gum is one of the rarest of extragenital chancres. In the majority of textbooks and atlases on dermatology and syphilis the subject is either not mentioned at all, or is dismissed with the statement that the lesion is a rare one. In Fournier's¹ volume "*Les chancres extra-génitaux*," and in Thouvenot's² "*These*," gum chancres are more comprehensively described than in any other report that I have been able to find in the literature. In Power and Murphy's "*System of Syphilis*" and in Zinsser's excellent atlas of oral syphilis the lesion is briefly mentioned, and in this atlas there is no illustration of this type of chancre. Indeed there is a great paucity of illustrations of gum chancre in the literature.

According to Thouvenot, the earliest recorded mention of gum chancre was by Astruc in 1736 and later in 1768 by Fabyre. The first recorded case report was in the same year by Swediaur. This writer records the case of a young woman who through an accident lost a tooth which a dentist replaced with a tooth extracted from an apparently healthy subject. Later the young woman developed a syphilitic ulceration at the site of the replaced tooth.

Reports of gum chancres by the older writers are difficult of analysis. Prior to the time of Rollet (1858), chancre was regarded as belonging to one of two types, one infected and the other noninfected. This view involved the well-known controversy concerning the unity and duality theories of chancroid and chancre.

In 1893, Bulkley³ collected 9,058 recorded cases of extragenital chancres from the literature, the localization of which, in part, was: 1,810 cases, or 19.9 per cent., were labial; 1,148 cases, or 12.6 per cent., were breast chancres; 307 cases, or 3.2 per cent., were tonsillar; 157 cases, or 1.7 per cent., were lingual; 42 or, 0.46 per cent., were gum chancres. In 1897, Muncheimer⁴ made an analysis of extragenital

1. Fournier, A.: *Les chancres extra-génitaux*, 1897, pp. 128-134.

2. Thouvenot, A.: *Etude sur le chancre des gencives*, Thèse de Paris, 1907.

3. Bulkley, L. D.: *Syphilis in the Innocent*, New York, 1894.

4. Muncheimer, F.: *Ueber extragenitale syphilisinfection*, *Arch. f. Dermat. u. Syph.* **40**:191-235, 1897.

chancres similar to that of Bulkley's analysis. In this analysis there was a total of 10,265 extragenital chancres, the localization of which was similar to that of Bulkley given in the foregoing.

The most recent and complete statistics on extragenital chancres are those of Scheuer.⁵ The analysis made in 1910 by this writer brought the total of extragenital chancres recorded in the literature to 14,590 cases. These were distributed, in part, as follows: 3,880 cases, or 26.5 per cent., were labial; 1,569, or 10.7 per cent., were breast chancres; 1,104 cases, or 7.5 per cent., were tonsillar; 273 cases, or 1.8 per cent., were lingual; 97 cases, or 0.66 per cent., were gum chancres.

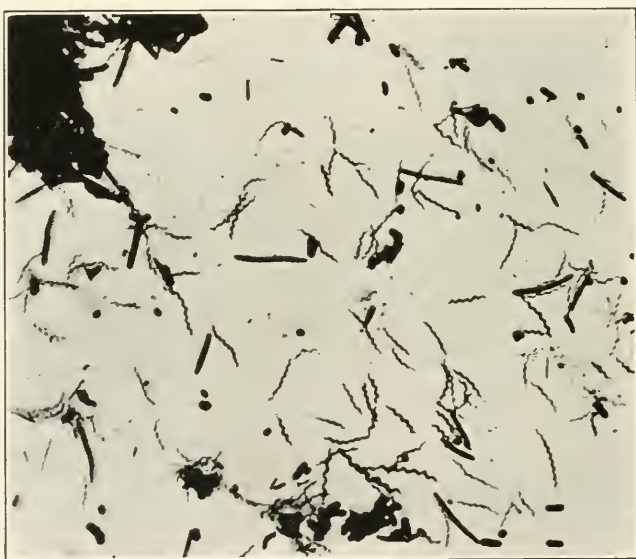


Fig. 2.—Smear made from normal buccal cavity, showing *Spirochaeta buccalis* (short coarse organism) and *Spirochaeta microdentium* (organisms with sharp curves) stained with Fontana stain: $\times 1080$.

The table is from Scheuer and gives the total number of extragenital chancres and their localization as reported by Bulkley, Muncheimer and Scheuer.

Since Scheuer's analysis in 1910, fifteen cases of gum chancres have been reported up to 1919, which makes a total of 112 cases of gum chancres reported in the literature.

According to statistics collected from different writers by Julien, of 1,977 chancres, 126, or 6.5 per cent., were extragenital; of the

5. Scheuer, O.: Die Syphilis der Unschuldigen, Berlin, 1910.



Fig. 1.—Chancre of the gum.

extragenital lesions, eighty-seven were cephalic, and of this number, seventy-three were buccal, of which only one appeared on the gum.

In an analysis of 2,185 chancres, Levy-Bing and Gerber⁶ found that 58, or 2.1 per cent., were extragenital. Of the extragenital chancres two were gum chancres.

THE TOTAL NUMBER OF EXTRAGENITAL CHANCRES REPORTED IN THE LITERATURE, WITH LOCALIZATION

	Bulkley, 1893	Muncheimer, 1897	Scheuer, 1910
Lips.....	1,810	2,285	3,880
Breasts and nipples.....	1,148	1,283	1,569
Oral cavity.....	734	751	824
Fingers and hands.....	462	522	897
Eyelids and conjunctiva.....	372	463	632
Tonsils.....	307	504	1,104
Pharynx and nasal cavity.....	264	290	423
Tongue.....	157	175	273
Chin.....	146	166	252
Cheeks.....	145	161	228
Trunk.....	100	124	168
Nose.....	95	125	172
Anus.....	87	108	176
Perigenital.....	77	80	278
Lower extremities.....	73	92	167
Forearm.....	59	60	79
Neck.....	47	51	63
Gum.....	42	57	97
Forehead and temples.....	37	50	69
Ears and scalp.....	27	30	52
Vaccination.....	1,863	1,872	2,144
Circumcision.....	745	746	753
Cupping.....	179	179	181
Tattooing.....	82	91	109
Total.....	9,058	10,265	14,590

In White and Brown's⁷ analysis of 19,000 cases of syphilis of all stages, there are 131, or 0.91 per cent., extragenital chancres. Of the 131 cases, 78 were labial chancres. A chancre of the gum was not observed in the series. The statistics of Levy-Bing and Gerber and of White and Brown were compiled solely from men, which, no doubt, explains the small percentage of extragenital lesions. Extragenital chancres are more common in women than in men. Fournier states that from 8 to 9 per cent. of all chancres are extragenital, and that they amount to about 22 per cent. of all chancres in women and less than 4 per cent. of all chancres in men. Indeed, in Borrie's⁸ analysis of 1,187 chancres in women, 27 per cent. were extragenital. This disparity in the two sexes mainly concerns the chancres of the breast, which occur almost exclusively in women. Moreover, in women

6. Levy-Bing and Gerber: 1,500 Cas de Chancres Syphilitiques Observés au Centre de Vénérologie de la Armée, Ann. d. mal. vener. **14**:321-340, 1919.

7. White, C. F., and Brown, W. H.: An Atlas of Primary and Cutaneous Lesions of Acquired Syphilis in the Male, London, 1920.

8. Borrie, J.: Les chancres extragenitaux chez la femme, Ann. d. mal. vener. **9**:31-39, 1914. (Five cases of gum chancres, cases previously reported.)

chancres occur more frequently in the mouth and in the region of the anus than they do in men.

It is apparent from these statistics that chancres seldom occur on the gum; yet the majority of all extragenital chancres are cephalic, but the majority of these are labial.

SOURCES OF INFECTION

Chancres existing in the mouth are more prevalent in some countries than in this. This is not to be attributed, as one might readily suppose, to perversion of the sexual act, but rather to the manner of eating and customs of different races, and to racial customs of nursing and



Fig. 3.—Smear from tonsillar crypt of normal person, showing *Spirochaeta vincenti* (long coarse organism), *Spirochaeta buccalis* (short coarse organism) and *Spirochaeta macrodentium* (small organism with sharp curves) stained with Fontana stain; $\times 1080$.

feeding children. This is particularly true among the lower classes in Russia. Indeed the possibilities of buccal infection with syphilis are well-nigh infinite, as is well shown by Fournier in his classic volume on extragenital chancres. In the reported instances of chancre of the gum, infection was apparently contracted in the following ways: through perversion of the sexual act (Montpellier and Lebon,⁹ Danlos,¹⁰

9. Montpellier, J., and Lebon, J.: Sur un cas de chancre syphilitiques. Simultanés de la gencive et du clitoris, Ann. d. mal. vener. **14**:219-220, 1919.

10. Danlos, M.: Chancre gingival, Ann. d. dermat. et syph. **6**:550-552, 1895.

Griffen¹¹); kissing (Kinsman,¹² Hulot, Haslund,¹³ Ledermann,¹⁴ Lieven¹⁵); use of appliances in the pursuit of different occupations (Gougerot,¹⁶ Levy-Bing and Clara¹⁷); various objects conveyed to the mouth (Gastinel and Legruin,¹⁸ Paul,¹⁹ Bruhns,²⁰ Nivet,²¹ Guladse²²); and through dental instruments (Levy-Bing and Clara, Roddick,²³ Lancereaux,²⁴ Chompret,²⁵ Fournier, Jeanselme,²⁶ Baer,²⁷ Kreibich,²⁸ Montgomery,²⁹ Neumann,³⁰ Roscher, Schaffer,³¹ Vajda^{31a}). Infected

11. Griffen, E. H.: Chancres Found in Unusual Localities, New York M. J. **63**:668-674, 1896. (Gum chancre contracted through an infected tooth brush.)

12. Kinsman, D. N.: Chancre of the Gum, Cleveland Med. Gaz. **2**:494-495, 1885.

13. Haslund, A.: Gum Chancre Contracted Through Kissing, Danish Dermat. Soc., March 5, 1902; Dermat. Ztschr., 1903, p. 535.

14. Ledermann, R.: Zur Bekämpfung der syphilis. Hygienisches Volksblatt, Vol. 3. (Forty-one cases of extragenital chancres; one gum chancre contracted through kissing.)

15. Lieven, A.: Die syphilis der oberen Luftwege, Klin. Vorträge aus dem Gebiete der Ootologie und Pharyngo-Rhinologie, Jena, 1898 (gum chancre contracted through kissing).

16. Gougerot, Levy and Clara: Deux chancres syphilitiques de Localisations Rares: Chancre Du Telephoniste et Chancre Du "Cuistot," Ann. d. mal. vener. **14**:148-151, 1919 (photograph of ulcerative chancre of the gum).

17. Levy-Bing and Clara: Deux cas de chancres gencive, Ann. d. mal. vener. **12**:221-224, 1917.

18. Gastinel and Legruin: Chancre de la gencive chez un edente, Bull. Soc. franç. de dermat. et syph. **8**:311, 1919.

19. Paul: Berl. Soc. Dermat., March 5, 1895; Ann. de dermat. et syph. **6**:816, 1895. (Gum chancre contracted through a drinking cup.)

20. Bruhns: Chancre of the Gum Contracted Through an Infected Cigarette, Berl. Dermat. Soc., March 1, 1897; Arch. f. dermat. u. syph. **45**:246, 1897.

21. Nivet, X.: Chancres syphilitiques extra-genitaux, Thèse de Paris. 1897.

22. Guladse, J. S.: Gum Chancre Contracted Through an Infected Cigarette, Arch. f. Dermat. u. Syph. **46**:468, 1898.

23. Roddick, T. G.: Rare Cases of Syphilis, Montreal M. J. **17**:93-98, 1888. (Six cases of extragenital chancre; one gum chancre contracted through tooth extraction.)

24. Lancereaux: A localization rares de la cavite buccale, Bull. de l'Acad. de méd., Par. **22**:447, 1889.

25. Chompret: Chancre de la gencive, Rev. de Stomatologie **7**:503, 1900; Bull. Soc. franç. de dermat. et syph. **16**:72, 1905.

26. Jeanselme, M. E.: Chancres extra-genitaux, Gaz. d. hôp. **79**:627-632, 1906.

27. Baer: Statistik über die in den Jahren 1897-1902 in d. B'schen Dermat. Poliklinik beob. Geschlechtskrankheiten. Festschrift anlässlich des 1 Kongress der Deutschen Ges. zur Bekämpfung der Geschlechtskrankheiten 1903 (twelve cases of extragenital chancres; gum chancre contracted through a tooth extraction).

28. Kreibich: Wien. dermat. Soc., April 12, 1899; Arch. f. Dermat. u. Syph. **49**:133, 1899. (Gum Chancre Contracted Through Tooth Extraction.)

29. Montgomery, D. W.: The Conveyance of Syphilis by Physicians, Calif. State M. J., **7**:218-220, 1905. (Three cases of extragenital chancres; gum chancre contracted through a dental instrument.)

toothpicks and toothbrushes are no doubt likely sources of infection; in fact, cases have been reported in which infection was conveyed through the toothbrush. The chief source of infection is perhaps not through venery, but is accidental. Most all writers mention dental instruments as the principal agent of infection. Dental instruments and infected toothbrushes are important agents, if not the principal ones. In the case herein reported there were two possible sources of infection. The patient was a homosexual type and admitted perversion of the sexual act; in addition, there was a history of a recent tooth extraction at the site of the chancre, and the time of extraction was consistent with the incubation period of the chancre.

SEX AND AGE

The majority of reported cases of gum chancre have occurred in adults, in men more frequently than in women. In Foveau and Courmelles'³² case gum chancre was seen in an infant and in Paul's case the patient was 75 years of age.

NUMBER

The lesion is usually, if not always, single. Indeed in all of the cases of gum chancre reported in the literature the sore was single. In one of Fournier's cases there was an associated chancre of the hard palate, and in Frossard's³³ case a lingual chancre. It may be recalled here that genital chancres are multiple to the extent of about 20 per cent. Multiple labial chancres are not uncommon.

LOCATION

In the cases reported gum chancres existed on all parts of both the upper and the lower gums. The anterior aspect of the gum is

30. Neumann, I.: Der extragen. syph. Primäraffekt in seiner klinischen und volkshygienischen Bedeutung, Wien. klin. Wchnschr. **15**:1001-1008, 1902. (Two hundred and seven cases of extragenital chancres; six cases of gum chancres, one contracted through a dental instrument.)

31. Schaffer, J.: Ueber ungewöhnliche u. diagnostisch schwierige Erkrankungen der Mundschleimhaut bei Syphilis und Hautkrankheiten, Arch. f. Dermat. u. Syph. **85**:371-436, 1907. (Gum chancre contracted through dental operation.)

31a. Vajda: Cases of Extragenital Syphilis, Pest. méd.-chir. Presse, 1896, No. 16.

32. Foveau and Courmelles: Infection syphilitique gingivale par une brosse à dents, J. d. mal. cutanées **17**:705, 1905.

33. Frossard: Des rapports entre l'état du système dentaire, Thèse de Paris, 1901. (Observation of a gum chancre coexisting with a lingual chancre.)

involved almost exclusively. In Bécèle's³⁴ case the site was a rare one, the posterior aspect of the superior gum above the median incisors being involved. The upper gum is more frequently involved than the lower one; the usual site of the chancre on the gum is opposite one or more canine teeth, sometimes the median ones but more usually the left lateral ones. It is interesting to contrast this usual site with the usual site of labial chancres, which is the right side of the upper lip.

LYMPHATIC INVOLVEMENT

The lymph nodes involved are those of the maxillary chain. The enlargement of these lymphatic nodes occurs early and is usually quite marked. The enlargement is painless, immovable and frequently of cartilaginous hardness, similar to the adenopathy accompanying labial chancre. This adenopathy may be the first or the chief subjective complaint of the patient. It is an important diagnostic aid.

TYPE OF CHANCRE

There are usually two types of chancres seen on the gum. The first, the abrasive or erosive chancre³⁵ is usually the earliest of the chancres on the gum to appear and to give rise to more or less characteristic clinical signs. The surface is more or less round, and it varies in size from that of a split pea, or smaller, to that of an almond; exceptionally, it is crescentic in shape. It is rather sharply demarcated from the surrounding tissue. The surface is smooth, of a beautiful carmine color, and owing to the liberal secretion of clear serum, it has a polished appearance. It is nonpainful but irritating foods and drinks, alcohol, condiments, etc., produce a sense of discomfort. When seen early, induration is absent. The chancre usually involves the gum just above the dental margin of one or two, less frequently three or four, teeth. The clinical recognition of this type is not difficult.

Exceptionally, the lesion described may remain unchanged, but usually the following changes occur, and the lesion then appears as a variety of the same type. The surface may become infected (abrasive infected chancre), and the lesion then becomes grayish or yellowish in color and is often covered with a pseudomembrane; or the center may become necrotic and ulcerated (abrasive ulcerative chancre); or induration appears with elevation of the previously flat erosion. The sore then appears as a raised mass (abrasive papular chancre). The chancre of

34. Bécèle, A.: Chancre syphilitique de la gencive à sa face interne, *Ann. de dermat. et syph.* 8:489-490. 1897.

35. The nomenclature of chancres employed in this paper is that proposed in the paper by J. V. Klauder, *The Early Diagnosis of Syphilis*, J. A. M. A. 72:693-699, 1919.

the case herein reported was of this variety and is shown in Figure 1. The erosive carmine colored surface may remain as such, or the surface may become infected with the subsequent changes described in the foregoing. The varieties of the abrasive or erosive character are typical clinically and are susceptible to clinical diagnosis.

The second type of gum chancre is an ulcerative type of chancre. This type is atypical, with no distinctive feature suggestive of chancre; it is therefore difficult to diagnose clinically. Indeed, as will be mentioned later, diagnosis by dark-field examination of this type is likewise difficult. It is seen as an ulceration of variable size and configuration. It may exist as small as a split pea; this, however, is uncommon, since the usual size is that of a ten-cent piece, or even as large as a quarter. At times it may be half-moon or crescentic in shape. The distinctive color, surface and edges of the erosive type of chancre are not seen in the ulcerative type. It is seen as a sharply circumscribed ulceration extending over the lingual surfaces of two or more teeth. This type of lesion is often irregular in contour with ragged edges, and its ulcerating surface gives off a pustulosanious discharge. The ulceration may expose the roots of the neighboring teeth or extend sufficiently deep to expose the periosteum. An infection of the periosteum not infrequently occurs, the symptoms of which make the diagnosis of chancre all the more difficult. Induration may or may not be present. The lesion is painful and tender.

DIFFERENTIAL DIAGNOSIS

Chancre of the gum is to be differentiated from inflammations and ulcerations due to a variety of causes affecting the gums and from tumors involving the gums. The distinctive clinical features of the erosive chancre and of its several varieties are rather characteristic, so that the differentiation of this type from other lesions is not difficult. In addition, the early appearing and usually extreme adenopathy is a valuable aid in differential diagnosis. Moreover, the Wassermann reaction and the dark-field examination constitute additional means of diagnosis. The differential diagnosis of the ulcerative type is considerably more difficult. The following considerations may serve in making the differentiation: the well-defined circumscription and rapid evolution of the lesion, and the history, if obtainable, that the sore appeared first as a superficial ulceration and later changed in character. The associated adenopathy, the Wassermann reaction and, to a less extent, the dark-field examination are valuable diagnostic aids. The recognition of *Spirochaeta pallida* in this type of chancre, as will be mentioned later, is difficult.

Chancres of the gum have frequently been diagnosed as one or the other variety of tumors which occurs at this region. In the case seen by Davis,³⁶ the lesion was diagnosed sarcoma and in one of Breda's³⁷ cases excision of the lesion was made, together with the adjacent teeth and part of the alveolus, on the supposition that the lesion was sarcomatous. In one of Gaucher's³⁸ cases the chancre was removed in the mistaken diagnosis of an epulis and in Rosenthal's³⁹ case for a malignant tumor.

Chancre of the gum may simulate in appearance these tumors which occur on the gum: fibroma, epithelioma and sarcoma. Fibroma arising from the gum or peridental membrane is styled fibroma epulis. This lesion is firm to the touch, and its surface is covered with mucous membrane. It is frequently sessile but may be pedunculated. It grows slowly but may attain a large size. It is nonulcerated, painless and not tender. It does not cause an enlargement of the lymphatic nodes. It may undergo myxomatous change or may become sarcomatous.

Epithelioma of the gum arises as a warty growth or as an indurated area which ulcerates early, or its primary appearance may be that of an ulcer. The ulceration is somewhat characteristic, especially the edges, which are raised and hardened. Its evolution and the adenopathy it produces are considerably slower than those of chancre.

Sarcomas, which are perhaps the most frequent tumors found in this locality, usually occur on the upper rather than on the lower gum. They appear as flattened masses at the edges of the gums which are not primarily ulcerated, but in which inflammation and ulceration may occur secondarily. Primarily, they are painless and not tender. Pain and tenderness, however, are present when the tumor is inflamed and ulcerated. The evolution of a sarcoma of the gum is considerably slower than that of chancre, and there is little tendency to metastasis and to lymphatic involvement.

DIAGNOSIS BY DARK-FIELD EXAMINATION

The demonstration of *Spirochaeta pallidac* in a gum chancre may be difficult owing to the presence in the oral secretion of spirochetes which are morphologically similar to *Spirochaeta pallida* (Fig. 2).

36. Davis, C.: Discussion of Smith's Paper, J. Cutan. Dis. **33**:691, 1915.

37. Breda, A.: Il sifiloma della gengive, Gior ital. d. mal. ven. **57**:7-13, 1916 (Four cases of gum chancre.)

38. Gaucher: Le Chancre et les syphilides, Paris, 1907. (One hundred and thirty-five cases of extragenital chancres; two cases of gum chancres.)

39. Rosenthal: Discussion of Paul's Case, Ber. Soc. of Dermat, March 5, 1895; Ann. de dermat et syph. **6**:816, 1895.

In the abrasive papular chancres, which are uninfected and nonulcerative, and the surface of which can be easily cleansed and saliva contamination prevented, *Spirochaeta pallida* can be easily demonstrated. Such was the case with the type of chancre herein reported. If, however, the lesion is ulcerated, the surface cannot be thoroughly cleansed, and the prevention of saliva contamination is less likely, so that the differentiation of pallida from other spirochetes becomes a difficult one. The presence of pyorrhea or thick tartar deposits also make this differentiation a difficult matter.

REPORT OF CASE

A man, aged 28, had all the earmarks of homosexuality and frankly admitted perversion of the sexual act—coitus ab. ore, in which he usually took the active part. The history was a typical one of homosexuality and need not here be detailed, except to state that he had practiced coitus ab. ore at rather regular intervals for a number of years.

About three months ago he paid several visits to a dentist, the latter finally extracting the left canine tooth. Soon after this the lesion on the gum appeared.

There was present a typical and well pronounced maculopapular syphilid and a generalized adenopathy. The cervical glands were particularly enlarged. A complete examination of the body failed to reveal any evidence of a chancre except the lesion on the gum. There were no mucous patches present.

The lesion on the left upper gum extended from about the midline to a short distance beyond the left canine tooth. It was nonpainful, not inflammatory, sharply margined and slightly raised. The lesion was of firm consistency, although the surface was rather spongy, not ulcerative, bright red, oozed serum freely and tended to bleed readily. The lesion resembled a nonpediculated epulis fibroma. Dark-field examination was positive.

The blood Wassermann reaction was + + + +. Both the gum lesion and eruption disappeared promptly under arsphenamin and mercurial treatment.

1922 Spruce Street.

SUSCEPTIBILITY TO DERMATITIS FROM RHUS DIVERSILOBA

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The word "immunity" is used in this article to designate the effective resistance of the organism against the principal, or most active, irritant in *Rhus diversiloba*. A high degree of immunity, therefore, designates a low degree of susceptibility and vice versa. Immunity is generally used to designate a low degree of susceptibility toward foreign protein. As the irritant poison of *Rhus diversiloba* is not a protein, the term is used in this paper to denote a natural or acquired resistance toward nonprotein substances, such as occurs with alcohol, chloroform, ether, atropin, cocain and opium. In this terminology, immunity includes what is commonly known as tolerance.

Judging by the evidence at present at hand, there seem to be two forms of immunity—natural and acquired.

NATURAL IMMUNITY

According to Kolmer, natural immunity is the resistance to infection normally possessed, usually as the result of inheritance, by certain persons or species under natural conditions.

This type of immunity to lobinol (the poisonous principle of *Rhus diversiloba*) is frequently relative and seldom, if ever, absolute. Persons are frequently found who are immune to lobinol when it is applied in the same concentration and condition as it exists in the sap of the plant, but when applied in a more concentrated form these persons are affected by it. Von Adelung,¹ in 1912, found that the concentrated alcoholic extract of *Rhus diversiloba* affected every immune person to whom it had been applied. Similar results were obtained by Warren,² in 1909, with *Rhus toxicodendrol*. Bibb,³ in 1914 and 1915, however, in experimenting with the sap of *Rhus toxicodendron*, found a person on whom it had no deleterious effect. Earlier immune results with the

1. Von Adelung, Edward: An Experimental Study of Poison Oak, M. A. Thesis, University of California (Nov.) 1912.

2. Warren, L. E.: The Poisonous Principle of Rhus, Pharmaceut. J. & Pharmacist, 4 S. 29:521 and 562, 1909.

3. Bibb, L. B.: Experimental Rhus Poisoning, Texas M. J. 30:162, 1914-1915.

sap of *Rhus toxicodendron* were noted by Kalm,⁴ in 1748, by van Mons,⁵ in 1797, and Blackwood,⁶ in 1880. I have observed similar cases with *Rhus diversiloba*. The sap of both the poison ivy and the poison oak has frequently been observed to have been transmitted from the hands and clothing of immune gardeners and those who have been working with the plants to others who were susceptible to it (Planchon,⁷ 1887; Busey,⁸ 1873; White,⁹ 1873; Lindley,¹⁰ 1908). Similar examples of relative immunity are found in experiments with bacteria and toxins on animals; for instance: rats are highly immune to diphtheria toxin, and readily withstand the effects of an amount equaling 1,000 lethal doses for a guinea-pig, but still larger doses may prove fatal; hedgehogs possess complete or almost complete immunity for the amount of snake venom deposited in an ordinary strike, but if venoms of several snakes are collected and injected at one time, death will result.

The commonly considered species immunity to rhus dermatitis in cases of the lower animals is frequently due to the protection of the skin by hair. White, in 1873, noticed that hunting dogs which have traversed woods infested with poison ivy are sometimes affected about the eyes. Kobert,¹¹ in 1906, stated that sheep and goats that eat the leaves and fruit of poison sumach (*R. vernix*) become sick and much harm results. Mackie,¹² in 1903, said:

On the ranges the leaves and berries (of poison oak) are readily eaten by sheep, goats, and horses, but not by cattle, as far as could be ascertained by observation and numerous inquiries. Many of the bushes are stripped entirely of leaves before they would naturally drop them.

4. Kalm, Peter: *Travels Into North America*, English tran., London, 1772, Ed. 2 1:53, 60-64, 139; 2:20.

Travels into North America. Trans. into English by John Reinhold Forster. In Pinkerton, John: *A General Collection of the Best and Most Interesting Voyages and Travels*, London, 1808-1814 13:402-403, 434, 1812.

5. Van Mons, J. B.: *Memoire sur le Rhus radicans*, Actes la soc. de méd. chir. et pharm. 1: part 2, 136-167, 1797.

6. Blackwood, W. R. D.: *Some Thoughts on Rhus Poisoning*, Philadelphia Med. Times 10:618, 1880.

7. Planchon, L.: *Accidentis causes par le contact du Rhus toxicodendron*, Montpellier Medical, 1887.

8. Busey, S. C.: *Poisoning by the Rhus toxicodendron*, Am. J. M. Sc. 17: 436-442, 1873.

9. White, J. C.: *On the Action of Rhus venenata and Rhus toxicodendron on the Human Skin*, New York M. J. 17:225-249, 1873.

10. Lindley, J. S.: *Rhus Poisoning*, Am. J. Dermat. & Gen.-Urin. Dis. 12: 342-344, 1908.

11. Kobert, R.: *Lehrbuch der Intoxikationen*, Stuttgart, 1906 2:511.

12. Mackie, W. W.: *The Value of Oak Leaves for Forage*, Bull. 150, California Experiment Station, Berkeley, California, 1903.

Pfaff,¹³ in 1897, when administering toxicodendrol per os to rabbits, noticed that it caused nephritis and death of the animals. Ford,¹⁴ in 1907, made similar statements. McNair,¹⁵ in 1917, cited one case in which a rabbit was given the sap of *Rhus diversiloba* per os, which caused albuminuria.

Many birds normally eat the fruits of the poisonous rhus.

It seems to be well liked by horses, according to interviews with United States government forest rangers. Jepson, in 1902, noted one observer, however, who asserted that "horses who feed on poison oak if driven until they become warm tremble and shake, and will die if not taken off the roads. Driven cattle are similarly affected."

Racial immunity is that type of natural immunity which exists among members of the same species. Dakin,¹⁶ in 1829, noted that mulattoes, negroes and Americans were equally susceptible to *Rhus toxicodendron*. French,¹⁷ in 1903, also stated negroes were not immune to *Rhus toxicodendron*. Lindley, in 1908, noted that the full-blooded Indians in California were immune while the half breeds were susceptible to *Rhus diversiloba*. Hrdlicka,¹⁸ in 1908, listed remedies for this dermatitis used by the Indians of the Southwest. Severe cases occur quite frequently in California among the Mexicans, Chinese and Japanese as well as among the native and foreign whites. There seems, therefore, to be no high degree of immunity existing among the principal types of races toward *Rhus diversiloba* or toward *Rhus toxicodendron*, as far as present knowledge extends.

Examples of individual immunity toward both infection by poison ivy and poison oak are not infrequent. All of these so far tested are relative and none are absolute.

There are many conflicting statements as to whether blonds are more susceptible than brunettes. Blonds, however, as far as I have

13. Pfaff, Franz: On the Active Principle of *Rhus toxicodendron*, Exper. Med. **2**:181-196, 1897.

14. Ford, W. W.: Antibodies to Glucosides, with Special Reference to *Rhus toxicodendron*, J. Infect. Dis. **4**:541, 1907.

15. McNair, James B.: The Pathology of Dermatitis Venenata from *Rhus diversiloba*, J. Infect. Dis. **19**:419-428, 1916. A Study of *Rhus diversiloba*, with Special Reference to Its Poisonous Properties, Amer. J. Botany, 1921.

16. Dakin, R.: Remarks on a Cutaneous Affection Produced by Certain Poisonous Vegetables, Am. J. Med. Sc. **4**:98-100, 1829.

17. French, J. M.: *Rhus toxicodendron* and *Rhus* Poisoning, Merck's Arch. **5**:223-5, 259-61, 1903.

18. Hrdlicka, Ales: Physiological and Medical Observations Among Indians of Southwestern United States and Northern Mexico, Bur. Amer. Ethnology, Bull. 34, 1908.

been able to ascertain, have never been said to be less immune than brunettes, but, on the contrary, always have been said to be more susceptible. The question, however, is of little value as both are affected in large proportions. Dakin stated that persons with light and dark skins were equally susceptible. Planchon regarded blonds as not more susceptible than brunettes. Lindley considered those with fair skins more liable to attacks than those with dark skins. Ward,¹⁹ in 1908, noted that brunettes were slightly less susceptible than blonds, although, he said, this observation was not to be relied on.

Horsfield,²⁰ in 1798, made the statement that females are more susceptible than males to *Rhus radicans*. In compiling the statistics of the cases of *Rhus diversiloba* dermatitis treated at the infirmary of the University of California for five years, the percentage of cases among males was less than the percentage of cases among females.¹⁵ This may be due to the fact that the skin of the female is generally more susceptible. The statistics, however, are not reliable for drawing these conclusions as (1) the total number of males and females exposed is not known, (2) the total number of males and females affected is not known, (3) the table shows only the number of students who came to the infirmary for treatment, which is not the total number affected, although it may be nearly the total number.

According to Baldwin²¹ (1887), fat people are more susceptible than thin people to the effects of *Rhus diversiloba*.

Some physicians believe also that children are less immune than adults (Horsfield, Dakin). There are cases in which the reverse condition holds true, as stated by Blackwood and by Cundell-Juler.²² It is quite probable that people, after reaching the age of 60 years, have a diminishing immunity in accordance with the general pharmacologic law.

Certain persons appear to possess a definite immunity to the poison or poisons, although they may be freely exposed for many years. In other persons immunity may increase or decrease. I have known of a forest ranger, in service in a California forest for many years, who

19. Ward, Ralph F.: Severe Ivy Poisoning, New York M. J. **88**:1224 (Dec. 26) 1908.

20. Horsfield, Thomas: An Inaugural Dissertation on *Rhus vernix*, *R. radicans*, and *R. glabrum*, Commonly Known in Pennsylvania as Poison-Oak, Poison Vine, and Common Sumac, University of Pennsylvania, 1798; C. Caldwell's Medical Theses, Philadelphia, 1805, p. 113.

21. Baldwin, A. E.: A Case of Poisoning by *Rhus toxicodendron*, Pacific M. & S. J. **30**:509 and 643, 1887.

22. Cundell-Juler: The Poison Vine, Cincinnati Lancet and Clinic **11**: n. s.: 73-76, 1833.

escaped infection, though he frequently was brought in contact with the sap of poison oak in clearing trails; finally he contracted the disease on returning to the habitat of the plant after a number of years' absence. Similar cases are of common occurrence in medical literature, especially in connection with poison ivy (Kalm, Dakin, Blackwood and Cundell-Juler).

Such variations of the degree of susceptibility in the same person may be dependent on the condition of the general health (Blackwood). Yandell,²³ in 1876, stated that enfeebled persons were most likely to be poisoned. The condition of the glands of the skin may have an influence, as has been previously considered (McNair²⁴). Horsfield considered persons more susceptible immediately after than before a full meal. Park²⁵ enlarged on this idea when he said that a "patient with an irritable skin, which reacts promptly to irritation in the digestive tract or elsewhere, should be particularly liable to annoyance from contact with such a pronounced irritant as *Rhus*."

There may be a relation between the sensitivity of the skin to *Rhus* and toward other irritants. Attacks of rhus dermatitis are known to have left a hypersensitivity toward sunlight and common English ivy (Stirling,²⁶ 1913). Perhaps the reverse holds true as well. Several persons immune to *Rhus* are greatly annoyed by mosquitoes while they are not bothered by fleas. On the other hand, one person who is quite susceptible to both *Rhus* and fleas is not appreciably susceptible to mosquitoes. Perhaps tolerance to *Rhus* may establish, or be the result of, a tolerance to other irritants of the same class as the prolonged use of alcohol creates a tolerance for chloroform. Chloroform and alcohol are considered to act on the same nerve cells and in the same direction.

Causes of Natural Immunity.—1. Various nonspecific factors may prevent infection. Among these may be mentioned the thickness and imperviousness of the skin, especially of the stratum corneum, and the physical action of the various secretions of the sebaceous and sudoriparous glands.

23. Yandell, L. P.: Poison Oak Eruption, Louisville Med. News **2**:32, 1876.

24. McNair, James B.: Pathology of Rhus Dermatitis, Arch. Dermat. & Syph. **3**:383, 1921. Lobinol-a Dermatitant from *Rhus Diversiloba*, J. Am. Chem. Soc., January, 1921.

25. Park, R.: Dermatitis Venenata; or Rhus toxicodendron and Its Action, Arch. Dermat. **5**:227-234, 1879.

26. Stirling, E. C.: An Eruption of the Skin Caused by the Poison Ivy, Australian M. Gaz. **33**:355-359, 1913.

2. The particular structure of the sebaceous and sudoriparous glands and the chemical nature and abundance of their secretions. This phase of the subject has previously been exhaustively considered in a previous article (McNair²⁴).

3. Phagocytosis may be of importance in natural immunity. Leukocytes may act either by engulfing and carrying away small particles of the poison, or their oxidizing and other enzymes may have a protective action against the poison.

4. A natural antitoxin immunity may exist. Although attempts to demonstrate such an immunity have never been successful either with lobinol, according to von Adelung (1912), or with toxicodendrol, according to Strickler²⁷ (1918), this failure may be due to the unsuitability of the present methods. Ford, in 1907, demonstrated the acquirement of tolerance in guinea-pigs and rabbits to six or seven times their minimum lethal doses, as well as the immune properties of the resultant serum. These experiments von Adelung was unable to repeat.

The chemical defense against lobinol may include oxidation, reduction, hydration, dehydration, substitution and addition. Such protective substances as may play a part may include carbonates, phosphates, protein, sulphur-containing substances and glucuronic acid. The probable phenolic nature of lobinol²⁴ would cause one to expect that it might form lobinol glucuronate and lobinol sulphate.

As iodine has the power to render lobinol nontoxic in vitro (Von Adelung, 1913), perhaps the thyroid secretion may play a part in susceptibility. It would be interesting to determine whether there is any relation between susceptibility and goiter.

There may also be substances present that do not chemically combine with the poison to render it physiologically neutral, but which antagonize it by stimulating other defense mechanisms, causing an antagonism similar to that which exists between chloroform and strychnin.

5. It may be that even after the introduction of the poison no great harm results because of a lack of suitable solvents or receptors on the part of the body cells of the host for the transmission or union of the pathogenic agent. The effect of the poison, therefore, may remain strictly localized to the point of immediate contact.

6. Immunity may be due to the absence of synergists, the absence of substances in the tissue that increase the toxicity of the poison.

27. Strickler, A.: Treatment of dermatitis venenata. *J. Cutan. Dis.* **36**: 327 (June) 1918.

ACQUIRED IMMUNITY

Acquired immunity may occur in two distinct forms: active and passive. A mixed type may exist.

Active Acquired Immunity.—Active acquired immunity is, according to Kolmer, that form of a resistance to infection brought about by the activity of the cells of a person or animal as a result of having had the actual disease in question, or as a result of artificial inoculation with a modified or attenuated form of the causative agent.

Such active acquired immunity may be found against rhus dermatitis when the defense mechanism of the body is stimulated by an attack of rhus dermatitis and antitoxic elaborations formed. Whether such a result is actually accomplished in rhus poisoning has often been questioned. Many observers assert that by chewing the leaves of the plant and swallowing the juice immunity can be acquired (Duncan,²⁸ 1916). I have not had an opportunity to experiment with such an immune person, but many cases are known in which susceptible persons who have followed these directions have been severely poisoned internally (Dakin; Conner,²⁹ 1907, and Alumbaugh,³⁰ 1903). I know of such cases in which the patient did not acquire immunity on recovery.

Another type of immunity may be caused similar to the common immunity toward nicotin. In acquiring such immunity by smoking tobacco the absorption of nicotin is not retarded nor its excretion accelerated, but the tissues become accustomed to small quantities of nicotin, and thus fail to react to it. Much of this tolerance is lost when the habit is discontinued, as in the case of opium.

Lindley states that "some persons doing manual labor are never free from the eruption entirely; it could be seen about the eyes, neck and wrists almost constantly." I contracted severe dermatitis several times from poison oak when about 13 years of age, but I have not been bothered with it since, although I not only frequently make trips into the habitat of the plant, but also rub the sap on my hands. Over a period of six years during which I have been experimenting with poison oak, I have always been able to produce local dermatitis in equally severe forms by applying the sap of the plant to the skin. The disease produced, although always mild, has never decreased in mildness with successive experiments. Strickler, in 1918, asserted that he had

28. Duncan, C. H.: Autotherapy in Ivy Poisoning, New York M. J. **54**: 901, 1916.

29. Conner, J. J.: Poisoning by Rhus toxicodendron, Am. J. Dermat. & Gen.-Urin. Dis. **11**:368, 1907.

30. Alumbaugh, W. E.: How Not to Do It, and Why! Rhus toxicodendron poisoning, Med. World **21**:176, 1903.

produced absolute immunity of short duration by the intramuscular administration of the poison.

There are many cases in which persons who have been able to handle any variety of poisonous *Rhus* with immunity on whom later a small amount of the sap would cause severe dermatitis (Kalm, Blackwood and Cundell-Juler). Persons who have frequently been subject to mild attacks may be liable to increased sensitivity, as shown in several University of California Infirmary cases (cases 4710, 4713, 4723, 5000, 5385).

The reverse has also been noticed. Horsfield, in 1798, stated that children are more readily poisoned than adults, and Dakin said that susceptibility recedes as age advances. I have known a number of people with a high degree of susceptibility which did not appreciably vary throughout a period of years. This opinion is supported by statements made by patients at the University of California Infirmary; for instance, the patient in Case 4536. Dr. von Adelung³¹ has also maintained a low immunity for a number of years.

Fluctuating degrees of susceptibility may occur in the same person, as shown in some of the cases of the University of California Infirmary (Cases 4814, 5665). Apparent changes in the degree of immunity may not always be actual for the severity of the dermatitis is governed, to a certain extent, by the amount of poison acting, as well as on the degree of resistance of the person.

Passive Acquired Immunity.—As the name indicates, this is a form of immunity that depends on defensive factors not originating in the person or animal protected, but is passively acquired by the injection of serum from one that has acquired an active immunity to the disease in question, according to Kolmer.³² Such immunity may perhaps result from drinking the milk of a cow fed on a mixture of grass and poison ivy plant, as cited by Dieffenbach,³³ 1917.

SUMMARY

In this paper immunity is used to include tolerance.

Natural immunity exists toward the principal irritant. It is usually relative and seldom absolute. Specie immunity exists among some animals and birds. As far as we know, racial immunity does not exist among Chinese, Japanese, Mexicans, negroes, the North American

31. Von Adelung, Edward: An Experimental Study of Poison Oak. Arch. Int. Med. **11**:148-164, 1913; Interstate M. J. **20**:139-142, 1913.

32. Kolmer, John A.: Infection, Immunity, and Specific Therapy. W. B. Saunders Company, Philadelphia, 1917.

33. Dieffenbach, W. H.: Treatment of Ivy Poisoning. South. Calif. Pract. **32**:91-92, 1917.

Indians or any other race. There are examples of individual immunity in which immunity is relative rather than absolute. Blonds and brunettes are both affected in large proportions. Females are apparently more susceptible than males. According to one writer, fat people are more susceptible than thin people. Age may influence immunity. There is no proof, however, that children as a class are more susceptible than adults. In the same individual the degree of immunity may vary or may remain constant. The degree of immunity is probably influenced by the condition of the health and the condition of the skin. Natural immunity may be due to: the thickness of the skin and the condition of the dermal glands, phagocytosis, natural antitoxin, lack of a suitable solvent or receptors for the poison, and an absence of substances in the tissues that increase the toxicity of the poison.

ACUTE SYPHILITIC NEPHRITIS

REPORT OF A CASE *

JOSEPH A. ELLIOTT, M.D., AND LESTER C. TODD, M.D.

CHARLOTTE, N. C.

Acute syphilitic nephritis is a condition reported infrequently and is especially rarely described in the American literature. Stengel and Austin¹ were the first ones in this country to give a comprehensive review of the subject; their work dealt largely with the chronic rather than with the acute cases. In 1916, Stokes² reported a case with a detailed review of the literature. He also reported another case recently, the etiology of which he questions. Cole³ reported a clear-cut clinical case in January, 1920, which fulfilled the usual diagnostic requirements. In a general discussion of syphilitic nephritis, Thompson⁴ called attention to a case that came under his observation, but he did not give details.

On the continent much more has been written on the subject of syphilitic nephritis. In 1900, Karvonen⁵ reviewed the literature and out of ninety-two case reports, he could accept only twenty cases as authentic. Fournier⁶ reported twenty-six cases from his own experience; Munk⁷ collected data of fourteen cases; Hoffman⁸ had seen six cases and Audrey⁹ reported two. Day¹⁰ added another case this year. In other words, acute syphilitic nephritis as distinguished from a slight transient albuminuria is a relatively uncommon complication

* From the Crowell Clinic of Urology and Dermatology.

1. Stengel, A., and Austin, J. H.: Syphilitic Nephritis, *Am. J. M. Sc.* **149**: 12, 1915.

2. Stokes, J. H.: Acute Syphilitic Nephritis, from the Standpoint of Diagnosis and Salvarsan Treatment, *J. A. M. A.* **66**:1191, 1916; A Note on Syphilitic (?) Parenchymatous Nephritis, *Am. J. Syph.* **4**:547 (July) 1920.

3. Cole, H. N.: Acute Syphilis of the Kidney, Report of a Case, *Am. J. Syphilis* **4**:46 (Jan.) 1920.

4. Thompson, Loyd: Syphilis of the Kidney, *J. A. M. A.* **75**:17 (July 3) 1920.

5. Karvonen, J. J.: Quoted by Stokes, *Dermat. Ztschr.* **7**:37, 183, 460, 770, 903, 1900.

6. Fournier, A.: *Traite de la Syphilis*, Paris **1**:735-741, 1901.

7. Munk, F.: Quoted by Stokes and Stengel and Austin, *Ztschr. f. klin. Med.* **78**: Nos. 1 and 2, 1913.

8. Hoffman, E.: Ueber akute syphilitische Nierenentzündung in der Frühperiode, *Deutsch. med. Wchnschr.* **39**:353, 1913.

9. Audrey, C.: *Ann. de dermat. et syph.* **3**:277, 1912.

10. Day, H. B.: A Case of Syphilitic Nephritis, *Lancet* **198**:1009 (May 8) 1920.

of syphilis. We wish to present the following case as illustrative of this unusual complication.

CASE REPORT

History.—Mr. S., an American, white, aged 30, married, an automobile dealer, was first seen Jan. 16, 1920. He complained of an eruption on the body and face with weakness and loss in weight. The family and personal history were negative. The present trouble began Dec. 5, 1919, as a slight urethral discharge. The last extramarital exposure occurred about three months before. He noticed a rash on his body ten days' previous to entering the hospital. His throat had been sore for three or four days. He complained of nocturnal pains in the shoulders, thighs and left side which had persisted for the past two weeks. During this time he had suffered with headache both day and night. He had lost about 20 pounds in weight during the five weeks preceding his entry, at which time his weight was 126 pounds. He had received no treatment.

Examination.—This revealed a rather poorly nourished man somewhat anemic in appearance. The scalp presented many pustular lesions covered by crusts. There were numerous papulopustular lesions on the forehead. The pupils were equal and reacted to light and in accommodation. On both tonsils were superficial ulcerative lesions which were covered with grayish pellicles. Over the entire body there was a profuse maculopapular rash, most prominent in the flanks, with scattered pustular lesions. There were confluent hypertrophic papulosquamous lesions on the shaft of the penis and around the anus. In the urinary meatus there was a lesion involving the entire opening. This lesion was distinctly indurated and had a serous discharge. There was a general adenitis. The tendon reflexes and the long bones were normal. There was no evidence of edema. The heart and lungs were negative. The spleen was not palpable. On entering the hospital the Wassermann reaction on the blood was strongly positive. The urine showed a large quantity of albumin, 7.5 per cent. by bulk (Purdy's centrifuge method), numerous large hyaline and lipid-appearing casts and a few small granular casts. The phthalein excretion was 56 per cent. in two hours. The blood urea was 58 mg. per 100 c.c.

Treatment and Course.—Stokes found in his experience that small doses of arsphenamin were most effective in these cases and attended with the least risk. Therefore, six injections, with a total dosage of 2.05 gm., were given at weekly intervals, the initial dose being 0.25 gm. Phthalein excretion and quantitative albumin determinations were made before each injection and again twenty-four hours later. The detailed findings are illustrated in the chart.

Albumin, Blood Urea and Phthalein Excretion Findings.—At the first examination the blood urea determination was 58 mg. per 100 c.c., which was twice the normal amount of blood urea. Probably this indicates some degree of nitrogenous retention. Previous to the fourth injection of arsphenamin it was less than 35 mg., but the last examination showed a rise to 48.5 mg.

The first phthalein excretion determination was 56 per cent. for two hours (39 per cent. during the first hour and 17 per cent. during the second hour). Although the patient had a marked nephritis, the phthalein excretion was practically normal. This observation has frequently been made in patients with acute nephritis. Apparently this holds true concerning those of syphilitic etiology as well. The phthalein gradually declined to an excretion of 46 per cent. following the second treatment. The excretion then increased until it reached 60 per cent., its highest point, which preceded the fourth arsphenamin

injection. Immediately following this there was a marked decrease in the phthalein output to 38 per cent. At the same time there was an increase in the amount of albumin in the urine. When the next entry was made the amount of phthalein was 50 per cent., but following the fifth treatment it declined again. The last two determinations before and after the sixth treatment were 32 and 34 per cent., respectively.

The quantity of albumin in the urine when the patient entered the hospital was 7.5 by bulk (Purdy's centrifuge method). Following the first injection of arsphenamin (0.25 gm.), there was an increase of the albumin to 10 per cent. The quantity was such that on heating, the urine coagulated so completely as to remain in the tube when it was inverted. This increase of 2.5 per cent. may be described as a manifestation of a Herxheimer reaction. Following this there was a rapid decline in the albumin content of the urine until just preceding the fourth treatment it reached 1 per cent. Following this treatment, it increased to 3 per cent. coincidently with a marked drop in the phthalein excretion. These facts suggest that the arsphenamin itself produced some damage to the kidneys and therefore the subsequent two doses were reduced in size. The next examination, a week later, showed only a trace of albumin and at the last three examinations the urine was entirely negative.

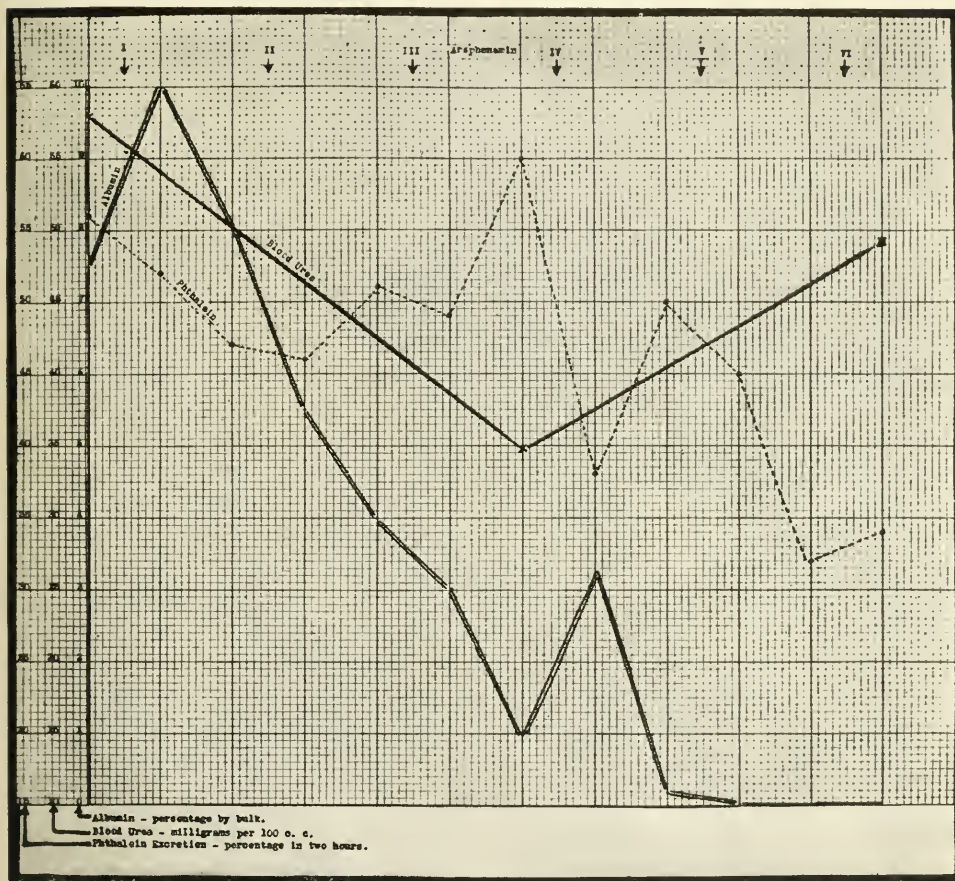
In regard to the presence of casts in the centrifuged sediment in this case, it should be noted that only on the entry examination and following the first treatment were they described as numerous, although even then they were disproportionately less in number than would be expected from the albumin content. Before the second injection they were less numerous and were even fewer in number after this treatment. From this point none were found at eight examinations.

GENERAL DISCUSSION

The onset in our case was gradual. The patient complained of a loss in weight of 20 pounds within five weeks and a progressive weakness. This is in accord with the majority of Munk's cases. The loss in weight was a prominent feature in our case, and one which was emphasized by Isaac as the most striking objective sign in his experience. Our patient did not show any evidence of edema which was so noticeable in Fournier's,⁶ Hoffman's⁸ and McDonald's¹¹ cases. Fournier also calls attention to the early tendency to uremia. Our patient did not show, on physical examination, any evidence of an impending uremia, but the urea content of the blood was decidedly increased (58 mg. per 100 c.c.). The impairment in health was by no means in proportion to the renal involvement, as evidenced by the albumin content. The number of casts was small in comparison to the amount of albumin. Some of them appeared to be lipid in nature; however, they were not examined with Nicol prisms to determine whether they were doubly refractile. These doubly refractile lipoids were first noted by Munk. This observer thought that the presence of these lipoids in the urine of nephritic patients was a diagnostic point of

11. McDonald: *Lancet* 2:207, 1915.

considerable importance in establishing syphilis as the etologic factor. Stengel and Austin, in this country, made a study of a series of nephritic patients with syphilis and another series without syphilis. They found these lipoids in six cases with a positive Wassermann reaction, while they found them in five out of fourteen patients who



Albumin, blood urea and phthalein excretion in authors' case.

did not have syphilis. They are led to believe from their studies that these lipoids are constant in cases of syphilitic nephritis, and while they frequently occur in other types of nephritis, they are not abundant.

DIAGNOSIS AND TREATMENT

The best recognized points in diagnosis, as described by Stokes are: (1) establishment of the existence of an early syphilis; (2) high albumin content of the urine; (3) double refractive lipoids in the

urine; (4) therapeutic tests. He believes that points 3 and 4 are the most reliable, while points 1, 2 and 4 are the most available. The existence of an early syphilis is usually established on physical examination; however, a Wassermann reaction is of value when the clinical evidence has disappeared. This is usually not the case unless the patient has received some treatment. The second requirement is met by a quantitative albumin determination. The third requirement, that of finding doubly refractile lipoids in the urine, is not diagnostic owing to the fact that these bodies are found frequently in nephritis of other origin. Furthermore, it may not be practicable because the average physician does not have available for use a polarizing microscope, as was true in our case. In our opinion the therapeutic tests are by far the most essential.

Both Stokes and Cole gave their patients initial mercurial treatments, and in each instance the drug produced toxic symptoms before the albuminuria disappeared. They later administered arsphenamin with the desired therapeutic effect. The specific treatment in our case consisted of arsphenamin injections followed by mercurial inunctions after the albumin had entirely disappeared. The initial dose of arsphenamin was 0.25 gm. followed by weekly injections of from 0.3 gm. to 0.4 gm. The first treatment was followed by a Herxheimer reaction with an increase of albumin from 7.5 per cent. to 10 per cent. The amount of albumin thereafter rapidly decreased, and no deleterious effects were noted until the fourth injection at which time the amount of albumin rose from 1 per cent. to 3 per cent. The dosage of arsphenamin was then reduced from 0.4 gm. to 0.3 gm., and the albumin entirely disappeared.

As the desired therapeutic effect may be obtained with 0.3 gm. of arsphenamin, it seems wise not to exceed this dosage until the albumin has disappeared from the urine.

CONCLUSIONS

1. Acute syphilitic nephritis is an infrequent complication of syphilis.
2. The diagnosis depends on: (a) the existence of any early syphilis; (b) the high albumin content of the urine with a relatively small number of casts; (c) therapeutic tests.
3. Our case fulfilled these requirements.
4. Arsphenamin is the drug of choice in treating this condition. An initial dose of from 0.15 gm. to 0.25 gm. may be given. The subsequent doses may be gradually increased. The maximum dose given our patient was 0.4 gm.
5. We believe that mercury should not be used until after the disappearance of the albumin from the urine, as advocated by Stokes.

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CURVE OF ONE THOUSAND FOUR HUNDRED
WASSERMANN REACTIONS AFTER TREAT-
MENT BY NEO-ARSPHENAMIN AND
MERCURY SALICYLATE

KEITH M. B. SIMON, M.B., L.M.C.C., D.P.H. (LOND.)

BELIZE, BRITISH HONDURAS

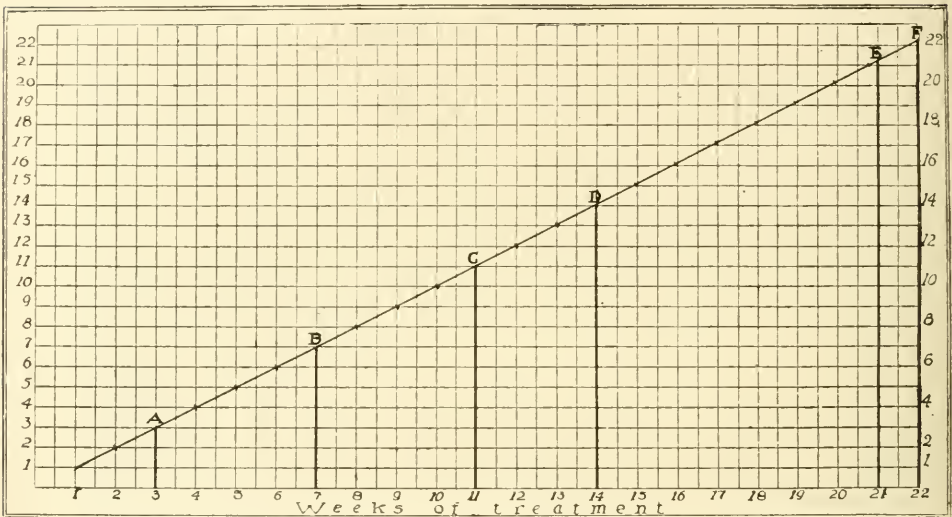
During the war it was the rule in the Canadian Expeditionary Forces that any one who had an entry of venereal disease on his medical history sheet must be treated in the venereal hospital, and that no patients would be returned to Canada unless they were non-infective. If possible, no patient was discharged from the clinic until a negative Wassermann reaction was obtained on the blood of the patient. Thus some patients with primary cases of venereal disease received eleven injections, and some with secondary cases received twenty-two.

AUTHOR'S METHOD OF TREATMENT

In our clinic the treatment consisted of at least seven weekly intravenous injections of neo-arsphenamin, beginning with a dose of 0.45 gm., and increasing it to 0.9 gm., and nine weekly injections of mercury salicylate (1 grain) in paraffin. The injection of neo-arsphenamin was omitted on the fourth and eighth weeks of treatment; on these dates the patients received only mercury salicylate injections. A point of great interest must be noted here. We dissolved the neo-arsphenamin in not more than 2 c.c. of freshly distilled water, the patients standing while the injections were given intravenously. We were able to do this at the rate of one injection a minute. We never had a case of fainting, vomiting or severe reaction while using this hyperconcentrated solution.

The Chart is compiled from 1,400 tests, about 700 patients being examined. A blood test was usually made on admission if the patient had not been tested serologically previously in some other laboratory. The second blood test was usually made after the primary lesions had disappeared in early primary cases, or on completion of the first course. If the patients gave a positive Wassermann reaction after seven injections of neo-arsphenamin and nine injections of mercury, at least a month was allowed to elapse before a second course was instituted. After obtaining a negative reaction these cases could not be further followed as the men were returned to their units or sent home for discharge. If a rash or secondary symptoms were also present, the case was considered a secondary one. The curve on the chart shows

that it took from two to eleven injections to obtain a negative Wassermann reaction in primary cases; secondary cases required from seven to twenty-two. The minimum number of injections for a primary case was two, for a secondary, seven; the maximum number of injections for primary cases was fourteen, and for secondary twenty-two. Tertiary cases never gave a negative reaction while under treatment in the clinic, but a diminution of fixation was invariably noted.



Wassermann reaction curve showing minimum and maximum doses of neoarsphenamin for change in reaction: A, minimum treatment to change a positive primary case to negative; B, minimum treatment to change a positive secondary case to negative; C, maximum treatment given to a patient with a primary case, the Wassermann reaction being positive; D, maximum treatment given to a patient with a primary case to change a positive Wassermann reaction to negative; E, maximum treatment given to a patient with a secondary case, the Wassermann reaction being still positive; F, maximum treatment given a patient with a secondary case to change a positive reaction to negative.

The technic¹ used for the Wassermann reaction was the No. 4 method recommended by the Medical Research Committee of the United Kingdom.

1. Medical Research Committee: Report of Special Committee on the Standardization of Pathological Methods. The Wassermann Test. Special Report Series No. 14. His Majesty's Stationery Office, March, 1918.

A SCHEME FOR PRESENTING THE SUBJECT OF THE INFLAMMATORY DERMATOSES TO STUDENTS IN TERMS OF FUNDAMENTAL CUTANEOUS REACTION SIGNS

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ROCHESTER, MINN.

In 1914, while teaching histopathology of the skin to medical students at the University of Michigan, I found it necessary in developing a dynamic comprehension of the field to lay stress on the fundamental pathologic unity which underlies the seeming diversity in the clinical pictures of the inflammatory dermatoses. In order to accomplish this purpose I analyzed the clinical picture of inflammation of the skin into nine component elements or cutaneous reaction signs, erythema, edema, vesiculation, oozing, crusting, scaling, lichenification, fissuring, and hyperpigmentation. Each feature of the clinically visible picture had its counterpart in some feature of the histopathologic picture. Subsequently at the University of Illinois I used a similar device to impress on students the distinction between acute and chronic dermatitis, on which therapeutic decisions so often depend.

In 1918 and 1919, in my lectures to the Fellows in the Mayo Foundation, I expanded the original scheme into the present attempt to picture the fundamental morphologic and pathologic unity of the inflammatory dermatoses. The nine cutaneous reaction signs constitute a keyboard, so to speak, on which by varying degrees of emphasis on individual notes or elements the "tune" or basic structural motif of any one of the inflammatory dermatoses from simple dermatitis through urticaria and pemphigus to psoriasis or an exfoliative erythroderma, may be played. It was not, in fact, until I had attempted such a scheme that I really appreciated for my own experience the conception of a limited group of fundamental reactions which represent the response of the skin to a wide range of etiologic agencies. A demand for reprints of the charts from those who seemed to find this schematization enlightening and valuable in impressing on them the morphology and interrelations of the dermatoses in question has emboldened me to offer the idea for criticism and suggestions from other teachers of dermatology.

(CHARTS)

The nine clinical elements of an inflammatory process in the skin and their equivalents in the pathology are represented in Chart 1 in the order of their appearance as the process passes from an acute to a chronic phase. The effort must be to teach the student to identify the individual elements in his cases, to estimate their proportionate share in the clinical picture, and then, by a process of reasoning rather than of mere visual memorizing, to recognize the inflammatory character and name the type and the stage of the dermatosis. Chart 2 represents the application of the general scheme to the analysis of dermatitis, and aims to give the student at one and the same time a conception of the morphology of eczema and of its alignment with dermatitis in general. Subsequent charts carry the analysis into other types. In Charts 2, 3, 4, and 5, the relative importance of the individual morphologic elements in the clinical picture is represented by variations in the size of the type. The boldest face is the most conspicuous or easily identified element in the dermatosis, the smallest type is the least conspicuous, or the rarest feature, or even entirely absent (such as vesicles in psoriasis). It will surprise a sophisticated dermatologist to see how seldom in his experience with such an analysis in mind even one of the nine elements will be found wholly and invariably absent from the clinical picture of any of the inflammatory dermatoses named. One has only to recall the description of vesicles in pityriasis rosea and urticaria pigmentosa, the clinical difficulty of distinguishing the Brocq type of parakeratosis variegata from premycotic mycosis fungoides, and the recently emphasized intermediate forms connecting urticaria with pemphigus by way of dermatitis herpetiformis, to realize, it seems to me, that the skin has only a limited range of reactions to a variety of pathogenic agents. These reactions manifest themselves in signs both clinical and pathologic, which when once identified by the student may form the basis of a rationalized physical diagnosis of cutaneous lesions. Such a mode of attack, even though imperfectly developed here, should be attractive to students because of its ability to introduce into a field, too often subject to the desiccating influence of quibbles on morphology, some stimulating conceptions of fundamental unity and evolution.

AN ANALYSIS OF THE INFLAMMATORY DERMATOSES BY MEANS OF NINE FUNDAMENTAL CUTANEOUS REACTION SIGNS BASED
UPON THE PATHOLOGIC CHANGES OBSERVED

CHART 1.—A COMPARISON OF THE MORPHOLOGY AND PATHOLOGY OF DERMATITIS

HISTOPATHOLOGIC CHANGES		CLINICAL MORPHOLOGY (CUTANEOUS REACTION SIGNS)
1 Vascular dilatation.	A C U T E	1 Erythema.
2 Edema, inter and intracellular. Cellular infiltration.		2 Edema (intumescence, papule or plaque formation).
3 Vesicle and bulla formation 1-with rupture. 2-without rupture.		3 Vesiculation or bulla formation.
4 and 5 Exudation.	S U B A C	4 Oozing.
6 Disturbance of the keratization cycle. Acanthosis. Parakeratosis.		5 Crusting from dried exudate.
7 Fibrous hyperplasia of cutis.		6 Scaling.
8 Cracking (mechanical)	C H R O N I C	7 Thickening and lichenification.
9 Proliferation of melanoblasts. Appearance of chromatophores in cutis.		8 Fissuring.
		9 Hyperpigmentation.
		(STOKES)

CHART 2.—ANALYSIS OF SIMPLE DERMATITIS

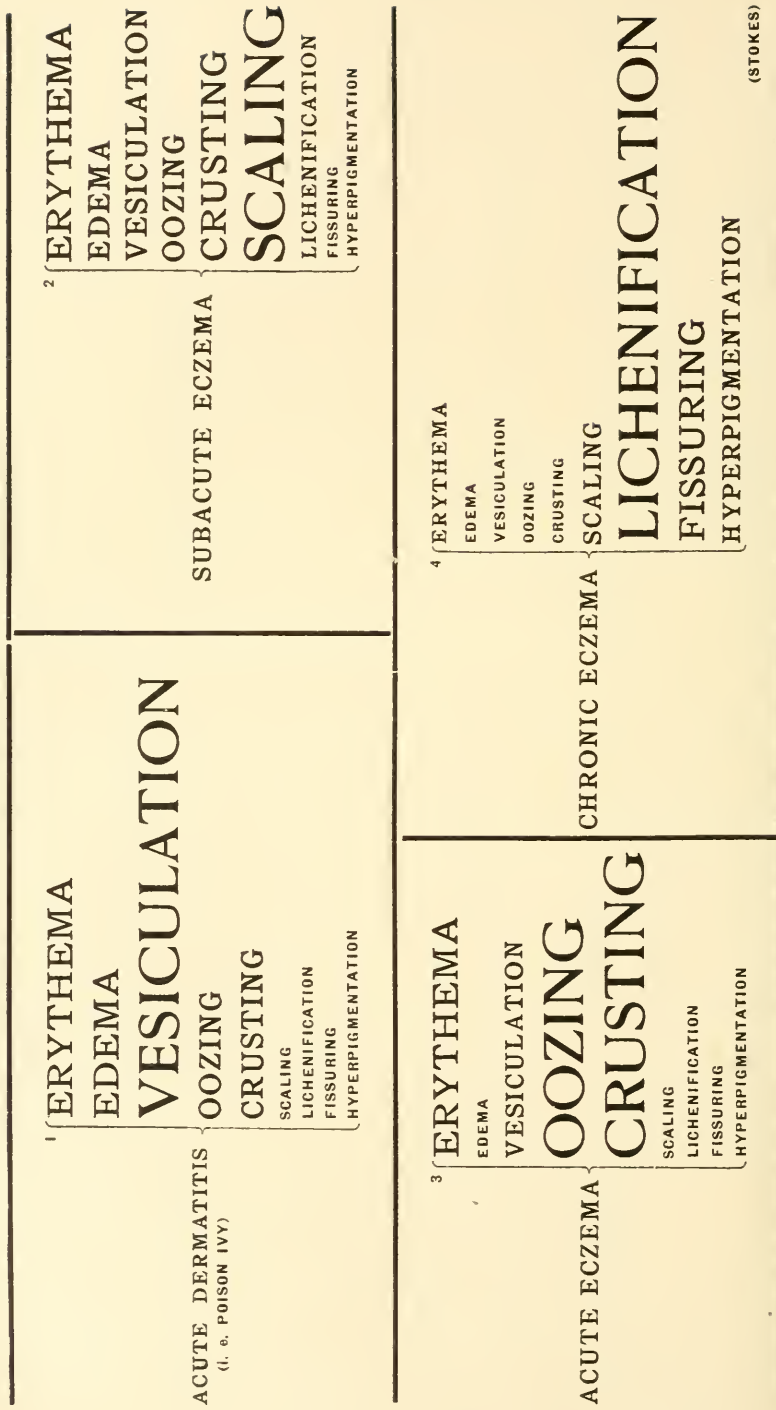


CHART 3.—ANALYSIS OF DERMATITIS OF PYOGENIC ORIGIN OR COMPLICATED BY PYOGENIC INFECTION

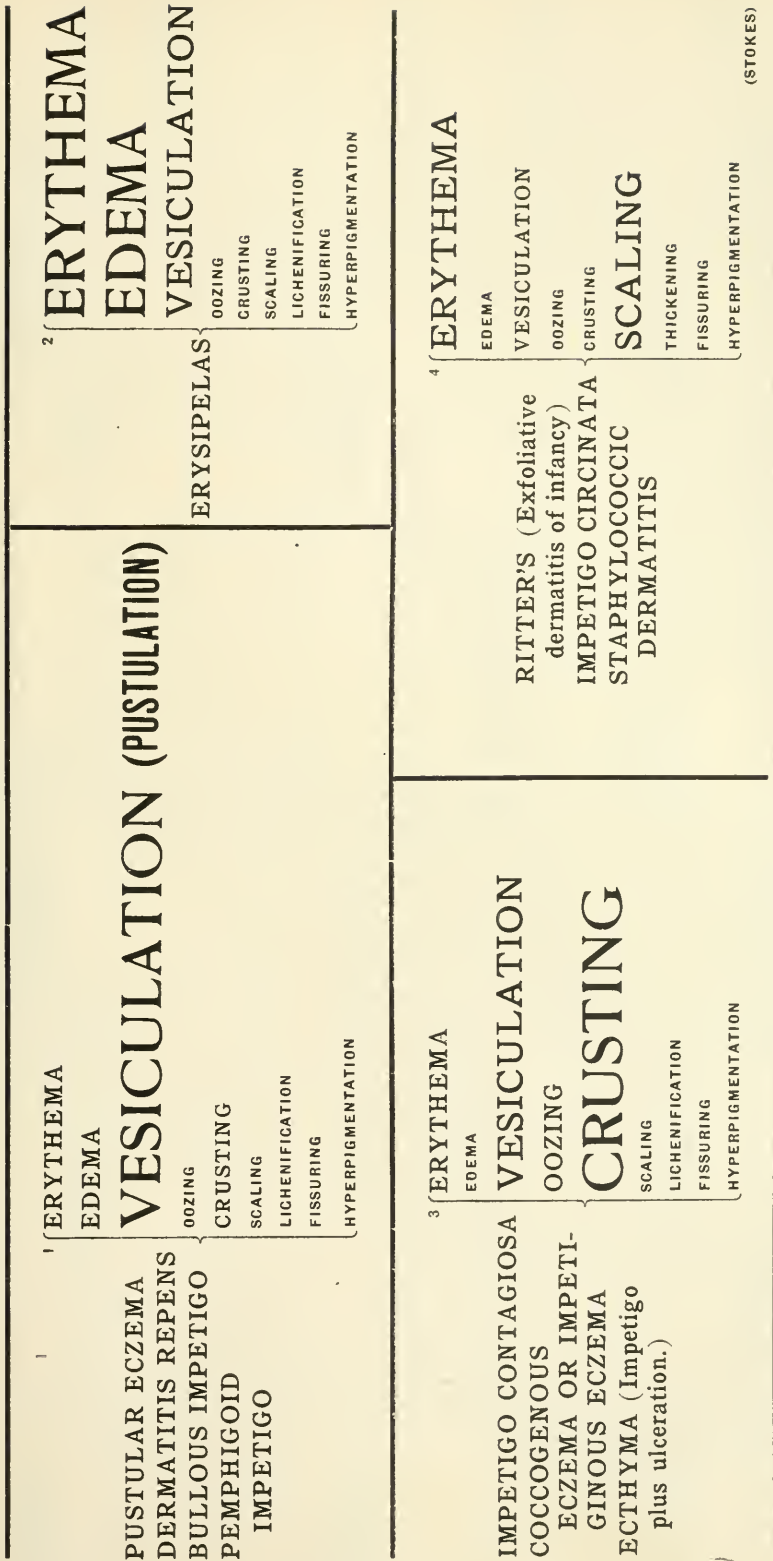


CHART 4.—THE TRANSITIONS FROM URTICARIA THROUGH ERYTHEMA MULTIFORME TO DERMATITIS HERPETIFORMIS AND PEMPHIGUS

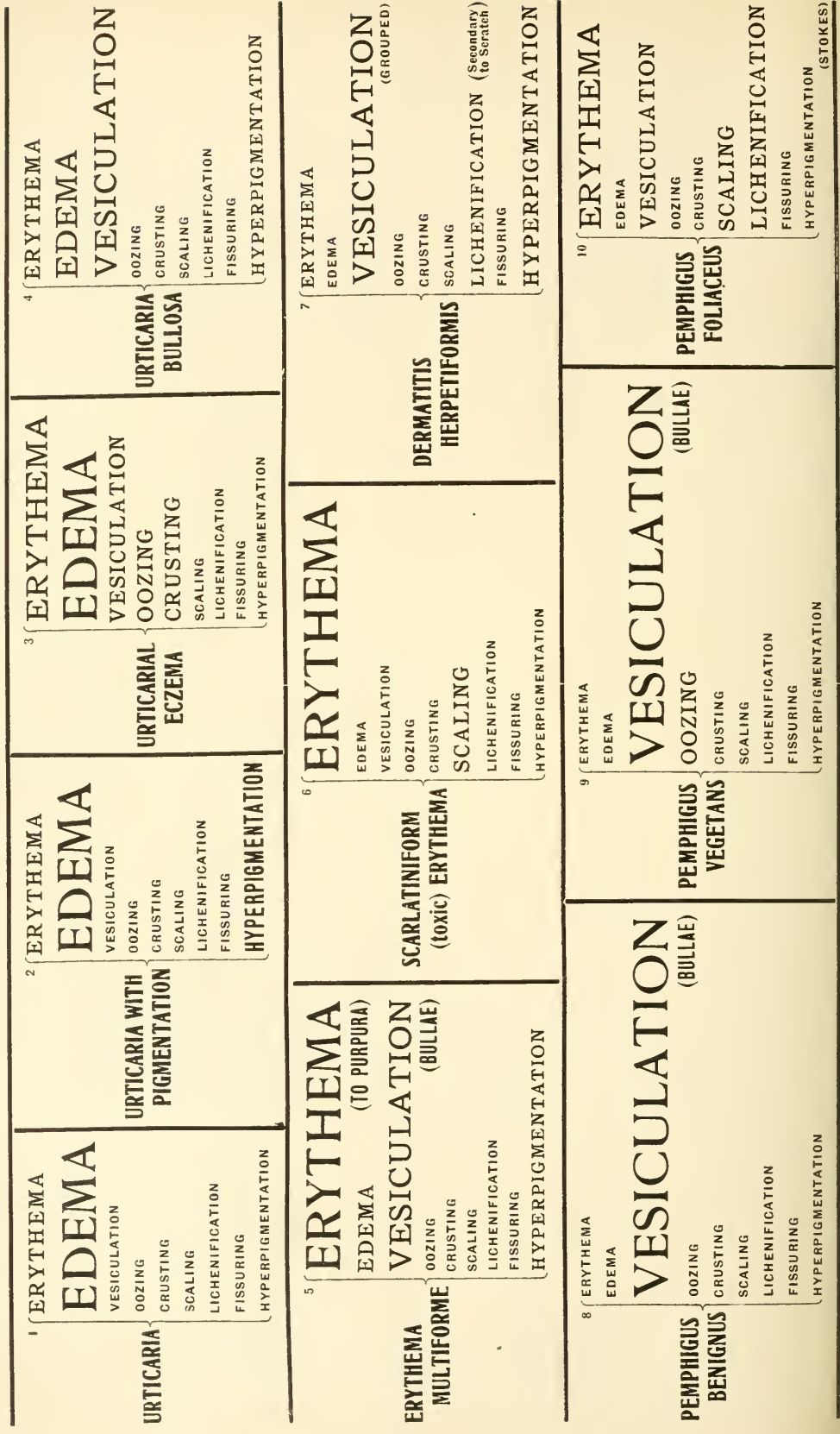


CHART 5.—ANALYSIS OF PSORIASIS, PARAKERATOSIS VARIEGATA AND THE EXFOLIATIVE ERYTHRODERMIAS

<div>1 { ERYTHEMA EDEMA VESICULATION OOZING CRUSTING SCALING LICHENIFICATION FISSURING HYPERPIGMENTATION }</div> <div>PSORIASIS</div>	<div>2 { ERYTHEMA EDEMA VESICULATION OOZING CRUSTING SCALING LICHENIFICATION FISSURING HYPERPIGMENTATION }</div> <div>PARAKERATOSIS VARIEGATA</div>
<div>3 { ERYTHEMA EDEMA VESICULATION OOZING CRUSTING SCALING LICHENIFICATION FISSURING HYPERPIGMENTATION }</div> <div>PITYRIASIS RUBRA HEBRAE PITYRIASIS RUBRA PILARIS</div>	<div>4 { ERYTHEMA EDEMA VESICULATION OOZING CRUSTING SCALING LICHENIFICATION FISSURING HYPERPIGMENTATION (STOKES) }</div> <div>LEUKAEMIC AND PSEUDOLEUKAEMIC ERYTHRODERMIAS, (leukemids) PREMYCOTIC MYCOSIS FUNGOIDES</div>

FURTHER INDICATIONS FOR PEPSIN-HYDRO- CHLORIC ACID TREATMENT *

E. H. AHLWEDE, M.D.

Assistant Physician

HAMBURG, GERMANY

As we have explained the fundamental idea of our pepsin-hydrochloric acid treatment in a previous article,¹ we wish to call attention to a series of further indications for this treatment, which we feel sure will be of practical use. The most important of these indications are: epididymitis, acne and strictures of the urethra.

A large number of patients with these conditions received pepsin hydrochloric acid treatment, which was applied in the form of (1) compresses, (2) injections, (3) ointment, and (4) guttaplasts. For compresses a 5 per cent. aqueous solution proved the most useful. For those who have not seen my first article, I repeat the following prescription:

	Gm. or C.c.
Pepsin	10
Hydrochloric acid	
Phenol	1
Water	ad 200

This solution applied in the manner I have already explained, gave excellent cosmetic results in the digestion of keloids; scars after burns and all kinds of cicatrices.

It was Unna's idea to inject pepsin in the following solution.

	Gm. or C.c.
Pepsin	10
Hydrochloric acid	
Phenol	1
Distilled water	100

In cases of gonorrheic epididymitis, in order to digest and soften the indurations of the epididymis, which are so often seen after acute inflammation, 5 c.c. of a 10 per cent. solution of pepsin were injected into the hardened tissue. The point of the needle was pushed through the tunica dartos up to the tunica vaginalis communis. After from three to four days, the irritation and swelling caused generally decreased, enabling us to continue the treatment and to make up to two injections a week. In new cases from three to four injections are sufficient. Old

* From the Dermatologic Clinic, Hamburg University, Professor Unna.

1. Ahlswede, E.: Digestion of Keloids, Cicatrices and Buboës, Arch. Dermat. & Syph. **3**:142 (Feb.) 1921.

infiltrations require regular injections over a period of from five to six weeks. It is advisable in these cases to combine the injections with the compresses of pepsin. Prophylactic compresses to avoid chronic induration in cases of acute inflammation of the epididymis were also used with success.

Callous strictures of the urethra were treated in the same way. As these represent an hypertrophy of the fibrous tissue usually situated in the pars bulbosa of the urethra, a bougie was first inserted, our pepsin solution (2 c.c.) was then injected into the tissues surrounding the induration. Externally we recommend that pepsin compresses with impermeable coverings be used at the same time.

For ambulatory treatment during the day a pepsin ointment has the advantage of easy application:

	Gm. or C.c.
Pepsin	10
Hydrochloric acid	10
Phenol	1
Petrolatum	100

In some cases the external application of pepsin and hydrochloric acid caused a slight superficial irritation of the skin due to the hydrochloric acid. This can be avoided by substituting boric acid. Unna's experiments showed that a 4 per cent. concentration of boric acid has practically the same digesting power as the hydrochloric acid combination. Strictly speaking, the effect is not quite the same, and this is a much milder treatment as hydrochloric acid causes considerable swelling of the collagenous tissue insuring the full attack of the pepsin, which is not quite attained by boric acid.

With regard to the digestion of keloids, scars and cicatrices, as explained in my previous article, I would like to add the following treatment for obstinate keloids and particularly for old cicatrices, for which our pepsin solution might prove too weak.

The old method of treating keloids, scars and cicatrices in our clinic consisted of the application of pyrogallol. As strong pyrogallol ointments will always cause an irritation of the surrounding skin, we restricted the pyrogallol effect to the keloids by applying it in the shape of a strong pyrogallol varnish. Thus two advantages were gained: (1) the surrounding skin was spared; (2) a certain pressure was exerted on the keloid, thus hastening the absorption; and (3) collodium in contracting opens up pores in the dried varnish allowing an active substance to pass through them—in this case pepsin-hydrochloric acid. The whole treatment therefore consists of two processes: the exact application of compressing pyrogallol varnish (applied with a thin brush) and application of compresses of pepsin-hydrochloric acid with impermeable coverings.

KELOIDS

The dressings are renewed once a day until the horny layer covering the keloids is worn off, and the surface begins to ooze. Treatment is then interrupted by an interval of a few days to restore the horny layer. We recommend that powder and a covering of Unna's zinc-gelatin then be used.

Though our treatment of keloids with pyrogallol and pepsin-hydrochloric acid works quicker than any other method recommended in this country, the treatment requires a certain length of time, according to the hardness of the keloid. A methodical and energetic treatment and patience on the part of the patient is necessary. The treatment may be interrupted at intervals and then continued in the same way until the cosmetic effect is attained.

TREATMENT OF ACNE

The hard nodes remaining after chronic cases of acne which have persisted many years, and which are troublesome to the patients, respond well to pepsin treatment. In acne we see the hard cicatrized collagenous tissue mixed with chronically suppurating follicles. The latter we generally puncture and then apply absorbing plasters, such as mercury-phenol or ichthyol plasters. The hard masses of the indurating acne are then covered with pyrogallol collodium, as mentioned in the foregoing, and the whole is covered with pepsin compresses.

COMMENT

The indications for our pepsin treatment are constantly spreading in this country, both with regard to the number of morbid conditions and to the different ways of application.

Correspondence

EPIDERMOPHYTOSIS PEDUM ET MANUUM

To the Editor:—The appearance of Arthur Whitfield's "Handbook of Skin Diseases and Their Treatment," provided an excellent impetus to abstract this subject to which the author's name has often been linked.

Eczematoid ringworm of the feet and hands (Epidermophytosis pedum et manuum) is described as a phase of epidermophyton infection in which the disease has become localized, most commonly between the toes, but also occasionally on the soles, the fingers, the palms and the nails.

In 1892, ringworm was found in dermatitis of the soles by Djellaludin Mouktar, but Sabouraud says that this was not the disease under discussion and Djellaludin Mouktar was of the opinion that the cases were of the eczema type on which a ringworm had become engrafted. In 1908, Whitfield found a series of cases in which the characteristic localization occurred, but he failed to grow the fungus. At that time he pointed out that it was not sufficient to make the diagnosis of intertriginous eczema between the toes, but that it was necessary to examine scales and the roofs of vesicles in order to determine the presence or absence of fungus. In 1910, Sabouraud, unaware of Whitfield's discovery, published an article on the same disease, and showed that it was due to *Epidermophyton inguinale*.

The characteristic localization of this disease is between the toes and up to the heads of the metatarsal bones. The eruption is marginate, but because of the complex arrangement of the toes, the circular outline is confused. Some times it may burst out as an apparently acute eczema with swelling and marked vesicle and bulla formation; at others, it may show as an indolent scaling with a few deeply seated vesicles at the edge. The clefts between the toes show a white, sodden, horny layer and a distinct margin runs in a more or less wavy line along the level of the heads of the metatarsal bones. Sometimes, ill-defined patches of vesicles and scaly dermatitis are present on the sole, especially in the hollow of the instep. The hands are affected in a manner similar to that of the feet. When the nails are affected, which is much less frequently the case, the brunt of the attack falls on the nail-bed, which develops a brownish hyperkeratosis, so that the nail plate is lifted off it. The nail plate itself may become reedy, discolored, and friable. Whitfield is not certain whether actual invasion of the plate itself occurs, as it is difficult to be certain whether the fungus found in scrapings lies in or on the nail plate.

Septic infection is common, and lymphangitis may occur, so that some patients have been treated for years for gout and gouty neuritis. The disease often becomes quite latent in cold, dry weather, resuming activity in hot and moist weather, when sweating occurs, so that there is a more or less seasonal variation, giving rise to the diagnosis of dyshidrosis.

The contagiousness is capricious, one patient having had the disease for over two years in one foot before the other became infected, although from ignorance as to its nature no active precautions had been taken.

When the infection has reached the toes the problem of treatment is difficult. The thick horny layer between the toes and the sole of the foot renders it almost impossible to get the parasiticide in contact with the fungus. Great care should be taken to trim away all flaps of fringed skin and to remove the roofs of any vesicles or pustules. Recent cases are much more easily cured than the old established and generally yield to ten days' treatment with chrysarobin ointment. In the treatment of old cases, Whitfield has used this method: The skin after trimming is painted with this solution:

R Chrysarobin	3 i
Sulphuric ether.....	
Acetone	5 ivss

This is allowed to dry, and then a pair of cotton socks is put on. In the evening the solution is washed off and the feet dressed with:

R Benzoic acid	gr. xxv
Salicylic acid	gr. xv
Soft paraffin	3 ii
Cocoonut oil	3 i

This does not stain the bedclothes but softens the epidermis. Next morning this is washed off, the skin trimmed again and the paint reapplied, after which a second pair of socks is put on while the first is being boiled. Even with this treatment the case may persist for months.

Another method that has occasionally been found useful is to soak the feet for ten minutes in a 2 per cent. watery copper sulphate solution and then without drying transfer them into a 1:20 dilution of the U. S. P. aqua ammoniae fortior, thus making ammono-cupric sulphate in the horny layer.

HERMAN GOODMAN, M.D., New York.

Abstracts from Current Literature

FURTHER PROGRESS IN THE STUDY OF THE RELATIVE EFFICIENCY OF THE DIFFERENT MERCURIAL PREPARATIONS IN THE TREATMENT OF CONGENITAL SYPHILIS IN INFANTS AND CHILDREN AS DETERMINED BY A QUANTITATIVE ANALYSIS OF THE MERCURY ELIMINATION IN THE URINE. WALTER R. RAMSAY and O. A. GROEBNER, *Am. J. Dis. Child.* **20**:199 (Sept.) 1920.

The treatment of syphilis with the different mercurial preparations is still haphazard, the rule being to give as much mercury as the patient will tolerate without salivation or diarrhea. Assuming that the amount of mercury eliminated in the urine during a given time would give a fair index of the amount in the circulation, Ramsay and Ziegler made some experiments and reported them in 1918. From these experiments they were able to conclude that, in infants and children, mercury, when given by mouth, by inunction or intramuscularly is excreted, at least partly, by the urine. In new-born infants and older children mercurial ointment, when placed in contact with the skin, without the use of friction, is taken up by the skin and excreted in the urine and continues to be excreted in the urine for a variable time after all treatment has been discontinued. By inunction (with rubbing) mercury is readily taken up by the skin and eliminated in the urine and continues to be eliminated for a considerable time. When one inunction is given, the maximum daily amount of mercury is usually eliminated during the following twenty-four hours, smaller amounts being eliminated for a variable time. When continuous inunctions are given, there is an accumulation in the system and considerable amounts are eliminated at intervals with only traces between. Mercury salicylate suspended in oil and given subcutaneously continues to be eliminated in appreciable amounts for eight days or longer, the daily amounts eliminated varying widely. Mercuric chlorid by intramuscular injection continues to be eliminated for eight days or longer. In all cases in which mercuric chlorid was used either by mouth or injection protein was found in the urine.

In a new series of experiments the authors sought to determine the amount and rapidity of absorption of the common mercurial preparations in use as determined by quantitative estimate of the amounts eliminated in the urine. Their deductions from this series of experiments were:

1. Mercurial ointment, 50 per cent., is to be preferred to the less concentrated forms and need not be repeated more than twice weekly instead of daily. The quantity of mercury absorbed is much increased by friction.

2. Calomel ointment is absorbed, but less rapidly and to a less extent than the mercurial ointment and should, therefore, be given in greater concentration.

3. The salicylate of mercury in oil should be given hypodermically twice weekly instead of once.

4. Mercuric chlorid given by hypodermic injection, although the dose is very small, continues to be eliminated for six or seven days. The fact that its use is frequently followed by the appearance of protein in the urine should exclude it from the treatment of syphilis in children.

5. Calomel by mouth is absorbed in small amounts and continues to be eliminated for a considerable time so that it is probable that it would be sufficient to give it at intervals of several days, thus avoiding diarrhea.

6. Gray powder is absorbed to a small degree and eliminated rather rapidly so that large doses repeated daily would probably be necessary to maintain mercury in the circulation.

OLIVER, Chicago.

ABSORPTION AND ELIMINATION OF MERCURY IN THE DIFFERENT METHODS USED IN THE TREATMENT OF SYPHILIS.

SVEND LOMHOLT, *Brit. J. Dermat. & Syph.* **32**:353 (Dec.) 1920.

Using a new and more sensitive method of determining the quantity of mercury in the urine and feces of the patients and animals receiving mercurial treatment by injection, inhalation, inunction and by various forms of intramuscular and subcutaneous injections, Lomholt adds some interesting data to the observations previously made on the subject.

In contrast to the general opinion that much more mercury is eliminated through the intestines than through the urine, the author found in over 300 cases that the quantity of mercury in the feces seldom exceeded that in the urine.

Some of the therapeutic conclusions reached were: The effect of mercury is due, in the author's opinion, to an indirect action through stimulation of the bactericidal forces in the human organism, since the concentration of mercury in the blood of patients undergoing full mercurial treatment is so feeble that a direct bactericidal effect is improbable. The aim of the treatment, therefore, should be to avoid all intoxication in order to avoid damage to the body and its bactericidal forces, but at the same time to maintain a sufficiently high permanent concentration of mercury in the organism without risking an intoxication.

During administration the slow elimination allows an increasing mercury accumulation in the body. But under a regular moderate supply the elimination can after a time reach an amount sufficient to establish a balance of absorption and elimination. In order to obtain the required saturation it is of advantage to make the supply of mercury somewhat larger at the beginning of treatment than afterward.

The daily amount of mercury that may be considered sufficient to cover the daily consumption (saturation and elimination) can probably be estimated at 6-10 mg. per day according to the size and tolerance of the patient, and the aim must be to find such methods of treatment as will provide a sufficient and regular supply to the organism. The curves of elimination show that this can be obtained by inunctions, by numerous small injections of soluble compound and by injections of calomel. Mercury salicylate does not seem absolutely reliable because its chemical composition makes it decomposable only with difficulty and because of its extremely rapid elimination. Metallic mercury has a serious drawback in its slow and sometimes irregular absorption, which may produce in some cases severe intoxication, in others a feeble therapeutic effect. Inunctions are reliable, effective and painless, but dirty and tiresome for the patient. Treatment with injections of calomel have always been estimated to be of great therapeutic value, but their painfulness prevents an extensive use. Injections twice weekly with 20 per cent. emulsion is effective in preventing pain.

The article is accompanied by a number of graphic charts showing the day to day elimination of mercury when used in the various forms.

SENEAR, Chicago.

BEMERKUNGEN ZU GENNERICH'S BROCHURE "DIE SYPHILIS DES ZENTRALNERNVENSYSTEMS, IHRE URSACHEN UND BEHANDLUNG" (REMARKS ON GENNERICH'S BROCHURE, "CENTRAL NERVOUS SYSTEM SYPHILIS, ITS CAUSE AND TREATMENT"). E. FINGER, Wien, klin. Wchnschr. **34**:33, 1921.

The brochure is a great and weighty indictment against the present practice of using mercury and arsphenamin in generalized early syphilis. This provokes syphilitic and metasyphilitic processes of the central nervous system, and is practically useless if the process in the central nervous system has been inaugurated. The frequent lumbar puncture required by treatment, which often requires 20 or 30 operations, cannot be accomplished except in a military establishment, or among educated persons who can be convinced of the necessity of the oft-repeated procedure. In ordinary civilian practice this is seldom accomplished.

The syphilologist and the neurologist must both be on the alert for the early recognition and study of cerebrospinal syphilis. Ways and means of best controlling the condition must still be devised. According to Finger, the problem which he proposed before the Neurological Congress at Frankfurt in 1911, whether early secondary syphilis should be treated with arsphenamin, and if at all, in what dosage, is again brought up by Gennerich's paper.

Gennerich has just published his results of the study of 8,000 cases, treated with mercury and arsphenamin. He has studied the cerebrospinal fluid and the nervous system of his patients. Among the figures quoted by Finger in his remarks are these: Pathologic findings accompanying pathologic fluids, 10 per cent.; no clinical evidence accompanying pathologic fluids, 90 per cent. Apparently also the mode of antecedent treatment is a great factor. The spinal fluid of 59.5 per cent. of untreated syphilitic patients was pathologic; the fluid of 30 per cent. of patients treated only with mercury and of 84.7 per cent. of patients treated with mercury and arsphenamin was pathologic. This preponderance of nervous system involvement was in a way anticipated soon after the release of Ehrlich's preparation.

Gennerich has frequently published observations on the treatment of his charges at the Marine Hospital at Kiel. His patients were chiefly young strong men. His brochure has chapters on other considerations of the problem of cerebrospinal syphilis which Finger does not include in his remarks.

GOODMAN, New York.

INTORNO AD ALCUNE QUESTIONI DI ANATOMIA MICROSCOPICA DELLA PELLE (CONCERNING SOME PROBLEMS OF MICROSCOPIC ANATOMY OF THE SKIN). L. MARTINOTTI, Gior. ital. d. mal. ven. **61**:597 (Nov. 30) 1920.

The author discusses the existence of a basal membrane in the epidermis, and from his own experiments concludes that there is no such membrane. In the upper part of the corium, the author says, the collagen and elastic fibers gather and form a tight stroma which by some staining methods appears as a separate membrane. The Herxheimer spirals of the epidermis are, according to Martinotti, true fibers from the corium which make their way among the epithelial cells. In the second part of his article the author proves the existence of a membrane in the epidermic cells, by means of a special staining procedure with azu-carmin and picrate of ammonium or magnesium. In the third part of his article the author discusses the subject of the origin of

keratohyalin. This substance, he believes, is a product of disintegration of the nuclei formed by a process similar to that described by Flemming, called chromatolysis. Sometimes true granules of keratohyalin are seen in the protoplasm, which undoubtedly come from the basophil substance that can be demonstrated in the protoplasm when stained with pyronin or Giemsa; in short, although keratohyalin comes mostly from the nuclei, a certain amount is derived from the basophil substance of the protoplasm. In pathologic circumstances a great deal of it may come from this last source.

V. PARDO-CASTELLO, Havana.

HERPES ZOSTER ALS EINZIGES MANIFESTES SYMPTOM VON IM UEBERIGEN LATENT VERLAUFENDEN ERKRANKUNGEN INNERER ORGANE (HERPES ZOSTER AS THE ONLY SYMPTOM IN OTHERWISE LATENT DISEASE OF THE INTERNAL ORGANS). ALFRED ARNSTEIN, Wien. klin. Wchnschr. **34**:13, 1921.

The relationship between herpes zoster and disease of internal organs has long been recognized. Girdle eruptions have long been associated with nerve disorders, tabes, neuritis; with metabolic disease—diabetes, uremia, gout; with intoxicants (especially arsenic); and finally with infectious disease—pneumonia, influenza, meningitis, sepsis, etc. In all probability, especially in the last group, one has to deal with a herpes simplex of unusual localization.

One of the most interesting forms of zoster to the internist is the so-called "reflex" herpes zoster, which is observed in various internal disturbances.

However, in all these cases the primary disease is in the foreground, and the zoster is merely an accidental observation. Hence it has seemed proper to record a number of histories of patients in whom the presence of herpes zoster led to diagnosis of internal disease which otherwise gave no symptoms. A right ninth dorsal herpes disclosed a swollen liver. There were no other subjective symptoms. After ten days the swelling had regressed sufficiently to allow the patient to leave the hospital. Other herpes zoster cases led to observations of lung affections, and other cases of liver disease.

On the other hand, it is admitted that many cases of zona were examined which did not disclose any derangement of internal organs.

The importance of routine physical examinations in cases of zona is to be emphasized.

GOODMAN, New York.

RECENT EXPERIMENTAL INVESTIGATIONS ON SYPHILIS. Berlin Letter, J. A. M. A. **76**:463 (Feb. 12) 1921.

Before the Berlin Medical Society, Geheimrat von Wassermann reported recently the results of his latest experimental investigations on syphilis. The error in the original conception of the reaction is admitted. It is well known that a positive reaction is not dependent on the presence of antigens derived from spirochetes or extracts of organs known to contain large numbers of that organism. But the practical value of the reaction has not been affected thereby; as with present-day antigens, it is positive in 90 per cent. of all cases of syphilis.

Wassermann's recent experiments were begun with the obvious assumption that the blood serum of syphilitic patients which constantly gave a positive reaction must contain some substance not present in the serum of persons unaffected with the disease. He has been able to demonstrate a body in positive serum, which in the presence of complement, enters into a reversible com-

bination with the extract used in the Wassermann test. The extract consisted of alcohol soluble lipoids derived from animal organs. The body present in syphilitic serums is produced by the lipid substance found in large amounts in the patients. Wassermann has proved that lipoids may cause the production of genuine antibodies, hitherto believed to be produced only in the presence of proteins. The Wassermann reaction can be explained as the result of the production of antibodies against the lipoidal substance; the latter, in turn, being produced in the body in large amounts as a result of the presence of spirochetes. The syphilitic patient shows an inversion (*Umstellung*) of lipid metabolism, which explains why the reaction is positive not only with extracts from the organs of all stillborn syphilitic children, but also with all organ extracts containing lipid-like substances.

Wassermann also expressed some of his views on the therapeutic aspects of syphilis. Mercury is effective principally because it acts on the cells that have been changed by the poison of the disease process and also on the inversion of lipid metabolism. Arsphenamin is purely spirillicidal in its effects.

MICHAEL, Houston, Texas.

A CASE OF HUMAN GLANDERS. F. H. JACOB, *Brit. J. Dermat. & Syph.* **33:39** (Feb.) 1921.

In Jacob's case the condition began with an indurated lesion on the wrist, apparently contracted from the infected udder of a cow. A series of secondary lesions appeared from time to time until the patient's death. These lesions were generalized, but involved particularly the limbs, back and flank. The skin lesions evolved rapidly, and involuted with equal rapidity, a single lesion running its course in a week. The throat was also involved, a large thick slough covering the left tonsil and the left half of the soft palate, the whole of this area appearing deeply ulcerated. This process resulted in extensive destruction of the involved parts. There was no sign of visceral involvement; the general health was fairly good, and a temperature of 100 to 102 F. was present. The patient was discharged with the mouth condition much improved, while the condition otherwise was unchanged. Jacob saw the patient four months later, when he had an extensive *cancrum oris*, and was in a bad general condition, and the cutaneous picture was about the same as before. The patient died a few days later. As the result of extensive laboratory work by H. M. Turnbull, J. A. Arkwright and G. M. Dobrashian, Jacob was able to prove the case to be one of human glanders. The pathologic findings are given in detail, and make a valuable source of information concerning the changes caused by the *bacillus mellei* in man.

SENEAR, Chicago.

ZUR ANWENDUNG VON INTRAVENOESEN INJEKTIONEN
HYPERTONISCHER TRAUBENZUCKERLOESUNGEN (METHODE
STEJSKAL) AUF DEM GEBIETE DERMATOLOGIE UND SYPH-
ILIS (EMPLOYMENT OF INTRAVENOUS INJECTIONS OF
GRAPE SUGAR [METHOD OF STEJSKAL] IN THE DERMATO-
LOGIC AND SYPHILIS SERVICE). VIKTOR PRANTOR, *Wien. klin.*
Wchnschr. **34:36**, 1921.

Intravenous injections of grape sugar in hypertonic solution (12.5 per cent.) has been advanced by Stejskal as having some action on the relation between blood and connective tissue. Prantor has given intravenous grape sugar injections in a number of patients followed in twenty hours by an injection of

either arsphenamin or mercury. No definite conclusions can be arrived at because the period of observation was small. He gives in outline the history of one of the syphilitic patients treated with 1 cm. of a 3 per cent. solution of mercury cyanid twenty hours after an injection of grape sugar (dose not mentioned). This patient is said to have been hard of hearing, and the disease process was one of the inner ear. Arsphenamin is said to have been contra-indicated. Hearing improved after the treatment outlined. The patient is supposed to have derived no benefit from a mercury arsphenamin course or from mercury-iodid treatment.

Another patient given iodids for psoriasis (according to Hasslund) was able to tolerate much greater doses after intravenous grape sugar injections. It appears that the injections of grape sugar intensify other medicine given. Other patients under observation have been similarly favorably influenced by this measure.

GOODMAN, New York.

SOPRA UN CASO DI SARCOMA IDIOPATICO DI KAPOSÌ OR ANGIO-ENDOTELIOMA CUTANEO (NOTES ON A CASE OF IDIOPATHIC SARCOMA OF KAPOSÌ OR CUTANEOUS ANGIO-ENDOTHELIOMA). G. BERTACCINI, *Gior. ital. d. mal. ven.* **61**:589 (Nov. 30) 1920.

The nature of this disease has not yet been definitely settled. Some dermatologists consider it as a form of sarcoma and others as a granuloma. The author reports a case with the following histologic findings: The corneous layer was atrophic in certain parts and hypertrophic in others with true parakeratosis; the interpapillary processes were entirely lacking or very small. The corium was invaded by a neoplastic mass in which numerous cavities filled with blood and lined with endothelial cells could be detected; these cavities were separated by a thick infiltration of numerous large round cells which the author thinks were endothelial; there were also masses of small round cells, especially around the blood vessels and the hair follicles. Plasma cells were scarce. Numerous granules of a brown pigment could be seen. The walls of the vessels were somewhat thickened. Fibrous tissue was found in large quantities enclosing the cellular elements in some of the old lesions. The tumors, according to the author, were of vascular origin, the process starting in the endothelial layer of the vessels. A clinical fact observed by the author was that many of the lesions became soft and fluctuating but never ulcerated or suppurated. In this case, the section of one of the tumors showed a cavity filled with blood and serum.

V. PARDO-CASTELLO, Havana.

X-RAY THERAPY. C. THURSTON HOLLAND, *Arch. Radiol. & Electroth.* **15**:199 (Dec.) 1920.

This article is the printed form of an address delivered before a body of general medical men and does not give the details of treatment and experience that are of such value to the expert. However, some of the author's statements may be of interest.

Roentgen-ray treatment is the treatment of choice in ringworm of the scalp. In all but a small minority of cases it is better to depilate the whole scalp according to the Kienbock-Adamson method. If Sabouraud pastilles are used to measure the dose, it is important to remember that they are only accurate when the tube is in proper condition of medium hardness. If the

tube is too high or too low the dosage will be wrong, even though the pastilles are colored correctly.

The roentgen ray should not be used to remove superfluous hairs. Even though the result may at first appear good, years later a disfiguring atrophy of the skin and telangiectasia will develop.

The author has had very gratifying results in hyperhidrosis and pruritis ani. In rodent ulcer, radium is better than the roentgen ray because it is easier to apply. This is particularly true when the malignant growth is near or on the eyelids. Occasionally a case is encountered which does not respond to radium or the roentgen ray. Holland does not believe that previous treatment, irrespective of the means used, has anything to do with this rarely observed intractability. It is inherent in the particular growth.

In squamous celled epithelioma, it is unjustifiable to treat with roentgen ray or radium alone, any case in which an operation is possible. Preoperative radiation should be done provided it does not materially delay surgical measures. Postoperative radiation is always advisable.

The author has found roentgenotherapy of value in exophthalmic goiter, tuberculous glands of the neck, Hodgkin's disease, splenic leukemia and in selected cases of uterine fibroids and menorrhagia.

MICHAEL, Houston, Texas.

A POLYNEURITIC SYNDROME RESEMBLING PELLAGRA ACRODYNIA SEEN IN VERY YOUNG CHILDREN. ALBERT H. BYFIELD. *Am. J. Dis. Child.* **20**:347 (Nov.) 1920.

In an interesting article the author reports seventeen cases of a disease which exhibited a definite resemblance to acrodynia or epidemic erythema. An uncommon clinical picture is described presenting marked sensory, and less marked motor, symptoms.

The cutaneous symptoms consisted of a nonconfluent erythematous rash of short duration which appeared on the fingers and toes, was most marked at the tips and faded away as it reached the wrist and ankle. The hands and feet were cyanotic and cold and in a few cases papules were superimposed on the erythema.

When the eruption disappeared, pigmented spots and desquamation followed. When the thorax or proximal portions of the arms and legs showed cutaneous manifestations, it consisted either of a morbilliform eruption or bullae.

Other changes noted were a pulling out and falling out of the hair, loosening of the teeth without any existing pathology being present, an extreme anorexia, frequency of urination, unusual sweating, and a leukocytosis ranging from 11,000 to 30,000.

It is thought that the disease is increasing; that infection rather than dietary errors seems to play the more important rôle as an exciting factor.

A postmortem examination in one case showed involvement of an occasional anterior horn cell, gliosis about the central canal and edema of the sensory roots.

It is suggested that the disease described is a postinfluenzal radiculitis or sensory polyneuritis.

OLIVER, Chicago.

THE URINE IN SYPHILIS. JOSEPH V. KLAUDER and JOHN A. KOLMER, J. A. M. A. **76**:102 (Jan. 8) 1921.

Urine examinations were made in forty-three cases of untreated primary syphilis, the duration of which was from a few days up to the time of cutaneous manifestations. Urinary abnormalities were present in three cases. The urine was examined in forty-six cases of untreated syphilis. Urinary abnormalities were present in four cases. The positive cases all showed albumin and granular casts, excepting two in which casts were absent. In two cases, red blood cells were present. The albumin consisted of a trace, except that in two of the secondary cases a light cloud was present with many granular casts, and in one red blood cells. The urinary abnormalities disappeared after treatment with arsphenamin and mercury. The clear blood serum and the urine, from the same patient, were mixed in order to ascertain the presence of precipitin or precipitogens in serum or urine. The serums and urine of twenty acute, untreated secondary cases were treated in this manner. The results were negative in all. Either the antibody is absent in the serum, or the antigen from the urine, or both may be absent, as indicated by the results. The Wassermann reaction was performed with the urine of sixty patients with syphilis in the different stages of the disease, many presenting acute symptoms and being untreated. Every patient yielded a positive blood Wassermann reaction, the majority of reactions being strongly positive with three different antigens. Of the sixty cases, the urine in but two yielded positive reactions. There is no characteristic feature in the urine of paroxysmal hemoglobinuria of syphilitic origin which serves to differentiate it from the same condition due to other causes. Results with urinary tests for syphilis were of no value as a means to diagnose syphilis.

WAUGH, Chicago.

THE DIAGNOSIS OF EARLY EPITHELIOMA OF THE SKIN. LOUIS SAVATARD, Brit. J. Dermat. & Syph. **32**:375 (Dec.) 1920.

Savatard calls attention to the fact that early epithelioma (prickle-cell carcinoma) of the skin is not usually diagnosed. The tumor can be diagnosed at least when it has reached the size of a pea, when it presents the color of the normal skin, elevation, a translucent appearance and small vessels coursing over its edge with its center apparently plugged. It is usually fairly hardened and infiltrates the true skin. The rapid rate of growth usually serves to distinguish it from rodent ulcer, which it simulates. Failure to extrude the "core" by ordinary pressure rules out molluscum contagiosum, while absence of inflammatory signs distinguishes it from a boil, and it should not be confused with a sebaceous cyst.

Two illustrations, one showing the site of a hundred primary epitheliomas and the others the site of a thousand rodent ulcers demonstrate that the lower lip and upper lid are frequently invaded by epithelioma and rarely by rodent ulcers, and that the bridge and tip of the nose are relatively more frequently the sites of epithelioma than of rodent ulcer.

A graphic chart shows the age incidence of scar epitheliomas, rodent ulcer and primary epitheliomas. In each group the youngest patient was 17 years of age. The rodent curve reaches its maximum at the forty-fifth year, the primary epitheliomas at the sixty-fifth year. Almost as many rodents began

between 17 and 45 as between 45 and 80 years, and epitheliomas are frequently seen in young adults. The scar epithelioma is a malignant growth of comparatively early adult age, for the new growth is related to the age of the scar and is independent of the age of the patient.

SENEAR, Chicago.

THE TREATMENT OF HEREDITARY SYPHILIS. PHILIP C. JEANS, J. A. M. A. **76**:167 (Jan. 15) 1921.

The author describes in detail a plan of treatment for hereditary syphilis which has been in use in the children's clinic of the Washington University Dispensary and in the St. Louis Children's Hospital for a period of four years. The child attends the clinic once a week. At each visit, 0.03 c.c. ($\frac{1}{2}$ minim) of a 1 per cent. solution of mercuric chlorid for each kilogram ($2\frac{1}{2}$ pounds) of body weight is injected intramuscularly. Mercury with chalk is prescribed three times daily by mouth in doses ranging from 13 mg. ($\frac{1}{8}$ grain) for small infants to 100 or even 130 mg. for the largest children. A laxative effect is avoided by decreasing the dose when necessary. Every two months a course of three intravenous injections of arsphenamin given at weekly intervals is started. The dosage is 0.01 gm. for each kilogram of body weight. Mercury administration is not interrupted for the arsphenamin course. A rest period of from four to eight weeks is given during the first year of treatment, provided the attendance has been sufficiently regular. Infants are required to continue such a routine for at least one year, and older children for at least two years, regardless of what the Wassermann reaction shows. Treatment is continued in the same manner for as much longer than this as seems indicated by the clinical signs or the Wassermann reaction. It has been found desirable to continue treatment for six months or longer after all evidence of activity, including the Wassermann reaction, has disappeared.

WAUGH, Chicago.

THE RED CELL BLOOD CONTENT OF THOSE HANDLING RADIUM FOR THERAPEUTIC PURPOSES. J. C. MOTTRAM, Arch. Radiol. & Electroth. **15**:194 (Dec.) 1920.

This article is one of a series of reports from the Radium Institute of London on the effect of radium on workers in that element. In a previous study, it was found that a leukopenia affecting both the polymorphonuclears and the lymphocytes was a common occurrence.

A similar investigation of the red blood cell count is reported. The author states that clinical and laboratory workers exposed to radium present, on the whole, a diminution in the number of red cells as compared to unexposed workers. However, the count fell within normal limits in most instances. Five exposed persons showed a moderate diminution of the red cell count and a high color index. These findings would be, perhaps, of only academic interest, were they considered apart from the three fatal cases accompanied by anemia that have occurred among the personnel of the Institute. Each of the fatal cases presented the features of an aplastic pernicious anemia. They were accompanied by a "leukopenia instead of a leukocytosis," thus simulating anemia produced by certain poisons, such as trinitrotoluol.

It would seem probable that the gamma rays of radium have a destructive action on bone marrow.

MICHAEL, Houston, Texas.

CARCINOMA OF THE EYELIDS TREATED WITH RADIUM. SANFORD
WITHERS, *Am. J. Ophth.* **4:8** (Jan.) 1921.

This is a report of eight cases with clinical findings, details of treatment and clinical photographs.

In these cases the clinical diagnoses were confirmed by the consultant staff of the Barnard Skin and Cancer Hospital of St. Louis. The exact details of the treatments being given, they lend themselves readily to translation or reduplication. Twenty-five and 50 mm. of radium element, in silver tube containers, were employed. Histologically the lesions were of the basal cell type of epithelioma. The results showed a high degree of therapeutic, physiologic and cosmetic success. Observations were made to the effect that associated cataracts and pterygia disappear under the influence of radium, that the sclera is particularly resistant to large doses and that the conjunctiva reacts more quickly and heals more rapidly than the lid epithelium.

FOERSTER, Milwaukee.

PORPORA EMORRHAGICA E TUBERCULOSI (PURPURA HEMOR-
RHAGICA AND TUBERCULOSIS). G. GARIN, *Riforma med.* **36:952**
(Oct. 16) 1920.

The association of purpura hemorrhagica and tuberculosis has been known since the reports of Rayer in 1827. Later, about sixteen authors have reported cases of purpura hemorrhagica in patients with acute or chronic forms of tuberculosis. The case reported by Professor Garin is that of a young man of 19 who after a sudden attack of multiple arthritis and pharyngitis, presented numerous hemorrhagic patches accompanied by marked swelling of the joints. The patient had also an acute nephritis manifested by the presence of albumin and casts in the urine. The condition of this patient grew rapidly worse; the urine became scarce, containing 12 per cent. of albumin; enterorrhagia occurred; the pulse became small, rapid and irregular; and the patient died on the twentieth day of illness. The postmortem examination showed tuberculosis of the lungs and numerous tuberculous glands of the mediastinum. The suprarenal glands presented numerous nodules of tuberculosis. The author believes that tuberculous toxins may be the cause of purpura, especially in cases in which the suprarenals are also attacked, and in hypofunction.

V. PARDO-CASTELLO, Havana.

CONDYLOMATA ACUMINATA. A. N. CREADICK, *J. A. M. A.* **75:1057** (Oct.
16) 1920.

Among the twenty patients studied by Creadick, ten gave a strongly positive Wassermann reaction. In five others with a negative Wassermann reaction the presence of gonorrheal infection was demonstrated by smears; in two the clinical history indicated a previous infection, but gonococci were not found. On the other hand, in three instances no evidence of gonorrhea or syphilis was obtained either from the history or from the clinical examination of the patient.

The treatment of condylomata acuminata is not likely to be sufficiently radical and thorough, and perhaps for this reason recurrences are frequently noted. The topical application of ointments and escharotics produces either a slow effect or none at all. Removal by cautery also is likely to be followed

by recurrence. Surgical excision offers the most efficient method of treatment. The larger growths may be amputated at the point of attachment of the pedicle, and the raw areas closed with cutaneous sutures; the smaller growths may readily be shaved off with a scalpel held at an appropriate angle. After removal of the smaller papillomas, bleeding is usually controlled by pressure; if not, the thermocautery will be effective.

WAUGH, Chicago.

ALOPECIA AREATA. H. W. BARBER, Brit. J. Dermat. & Syph. **33**:1 (Jan.) 1921.

Barber states that in his opinion alopecia areata is due usually, if not invariably, to, focal infection. He has collected evidence to show that the streptococcus longus is the usual infecting organism, but it is quite possible that others may sometimes be responsible. He indicates that alopecia areata may be a chronic anaphylactic phenomenon, the antigen being bacterial protein, absorbed from the teeth, tonsils, nasopharynx, etc.

In treatment the most important thing is to remove, as far as possible, every source of infection. Vaccines are used in addition. For the anemic, iron and arsenic are given, and dilute hydrochloric acid when hypochlorhydria exists, and other methods of internal medication are mentioned. Pure phenol or lysol is suggested as the best agent to improve the blood supply through irritation.

There is an added note on the estimation of pathogenicity of the tonsil, written by A. M. Zamora.

SENEAR, Chicago.

HISTOLOGICAL CHANGES IN THE BONE MARROW OF RATS EXPOSED TO THE RADIATIONS FROM RADIUM. J. C. MOTTRAM, Arch. Radiol. & Electroth. **15**:197 (Dec.) 1920.

Rats were exposed to the gamma rays of radium for from 12 to 460 hours. Under the conditions of the experiment a twelve hour exposure was equivalent to $\frac{1}{1000}$ th of a rad.

The bone marrow of the femur was then studied histologically and compared with suitable control sections. Only specimens from rats that had been exposed more than forty-eight hours showed any decided differences from the controls. The changes consisted in a decrease in the number of mitoses and in a diminution in the number of young recently divided and darkly staining nuclei, and of nuclei in the anaphase.

These findings explain the blood changes observed in radium workers.

MICHAEL, Houston, Texas.

PROPHYLAXIS OF SYPHILIS WITH ARSPHENAMIN. LEO L. MICHAEL and HERMAN GOODMAN, J. A. M. A. **75**:1765 (Dec. 25) 1920.

The authors call attention to a method of preventing syphilis which they have found efficacious and which has not previously been described in the American literature. The injection of arsphenamin in small doses into persons who present no lesions, and who are definitely known to have been exposed to syphilitic infection, has in all cases resulted successfully in acting as a prophylactic measure. The prophylactic doses have averaged 0.3 gm. of arsphenamin, and the number and interval of the injections have varied with the time since the first exposure. In no case has less than three doses been

given. The time since exposure has little bearing on the result, but must be taken into consideration when the details of the procedure are under consideration. In two reported cases a single injection has been held to be ample.

WAUGH, Chicago.

THREE CASES OF ICHTHYOSIS FOLLICULARIS. MALCOM MANSON, Brit. J. Dermat. & Syph. **33**:20 (Jan.) 1921.

Manson described three cases of baldness occurring among eight children in the same family, and stated that they seem to fall under the same category as three cases reported by MacLeod under the name "Ichthyosis Follicularis Associated with Baldness." In Manson's cases the condition was peculiar in that it was limited to the head, and did not show the same degree of follicular hyperkeratosis as in MacLeod's description.

The only point of interest in the search for a possible etiology was the discovery that the mother had eczema of the vulvae during each of the three pregnancies from which these children resulted, while in her other pregnancies she had no eczema.

SENEAR, Chicago.

CASE OF DELHI BOIL. A. CASTELLANI, Proc. Roy. Soc. **14**:1 (Jan.) 1921.

A soldier who had served in India developed boils on his left forearm. Scrapings from the nodules revealed numerous leishmanias. The case was presented on account of the presence of atypical lesions, and the unusual occurrence of general symptoms and enlargement of the liver and spleen. Dr. Castellani stated his belief that cutaneous leishmaniasis, even in mild form, is not merely a local infection, but that there is a general infection, and therefore he preferred the intravenous use of tartar emetic.

GUY, Pittsburgh.

ANTHRAX IN ANIMAL (HORSE) HAIR. S. DANA HUBBARD, J. A. M. A. **75**:1687 (Dec. 18) 1920.

Details of a campaign against the menace of anthrax are given as carried out in New York City where, in the last seventeen months, there have been reported to the division of industrial hygiene of the department of health thirty-four cases of human anthrax, of which eleven have been fatal. A campaign of education of those engaged in the manufacture of brushes, particularly those using horsehair, was undertaken in order to secure general cooperation in an endeavor to annihilate this modern industrial and public health menace at its source.

WAUGH, Chicago.

ETIOLOGY OF TSUTSUGAMUSHI DISEASE. N. HAYASHI, J. Parasitol. **7**:53 (Dec.) 1920.

The author has been studying this disease for over twelve years and gives in this article a summary of his findings.

Tsutsugamushi disease occurs in Japan along the rivers of the northern provinces. It has a close resemblance to Rocky Mountain spotted fever. The clinical course is marked by a gradual rise of temperature, a characteristic lesion at the site of the bite, and swelling of the adjacent lymph nodes. It is transmitted by a minute red mite, *Leptus akamushi* (Brumpt), which is ecto-

parasitic in the ear of field mice, but attacks human beings and other animals if they are accessible. The death rate of the disease is 40 per cent.

Hayashi's studies enable him to conclude that the disease is due to a protozoal organism which he designates tentatively as *Theilceria tsutsugamushi*. Cultural experiments have been negative.

MICHAEL, Houston, Texas.

AZIONE IN VITRO DEL NEOSALVARSAN SUI BACILLI DEL CARBONCHIO DA COLTURA E SUI BACILLI PROVENIENTE DELL'ORGANISMO ANIMALE (THE ACTION OF NEO-ARSPHENAMIN ON CULTURES OF ANTHRAX BACILLUS AND ON THE BACILLUS OF ANIMAL ORIGIN). F. TALLO, *Riforma med.* **36**:1145 (Dec. 11) 1920.

In 1912, Bettman and Becker used arsphenamin in three cases of human anthrax with complete success; their patients recovered in a short time. Tallo has studied the effect of neo-arsphenamin on *Bacillus anthracis* in vitro and arrives at the following conclusions: 1. Neo-arsphenamin added to cultures in broth of noncapsulated *Bacillus anthracis* has intense and rapid bactericide properties. 2. The same results are obtained with cultures in blood serum. 3. Under the same conditions, capsulated *Bacillus anthracis* of animal origin are not affected by neo-arsphenamin.

V. PARDO-CASTELLO, Havana.

ARSENICAL KERATOSIS AND EPITHELIOMA. G. R. HAMILTON, *Brit. J. Dermat. & Syph.* **33**:15 (Jan.) 1921.

Hamilton's patient, a woman 46 years of age, had taken arsenical solutions at least nine months each year for thirty-six years and developed various cutaneous and neural changes as a result. In January, 1919, she developed two pinhead sized spots on her right arm. These gradually grew larger, and a squamous and horny carcinoma of the form of a malignant papilloma was formed. The patient was sure that she had never had a lesion of psoriasis at the site of the carcinoma. Arsenic was found by Marsh's test in the skin, urine, hair and nails.

SENEAR, Chicago.

AN EXPERIMENTAL STUDY OF THE LATENT SYPHILITIC AS A CARRIER. FREDERICK EBERSON and MARTIN F. ENGMAN, *J. A. M. A.* **76**:160 (Jan. 15) 1921.

This is an interesting report of the study and work done by the authors. A detailed description of the experiments is given. *Spirochaetae pallidae* were isolated in five instances from patients with latent syphilis—three times from the inguinal glands and twice from the serum. The virulency of the different strains for rabbits, was retained. The blood and spinal fluid did not prove to be infectious. These investigations demonstrate the fact that those persons that give a history of an old syphilitic infection may harbor virulent *Spirochaetae pallidae* for years in spite of irregular negative Wassermann reactions or slight reactions only in the cholesterin antigen.

WAUGH, Chicago.

NEW CONCEPTIONS RELATIVE TO THE TREATMENT OF MALIGNANT DISEASE WITH SPECIAL REFERENCE TO RADIUM IN NEEDLES. W. L. CLARK, *Am. J. Electroth. & Radiol.* **39**:1 (Jan.) 1921.

In this comprehensive article Clark discusses the necessity of cooperation between those who use different methods of treating cancer, such as surgery,

radiotherapy, electrocoagulation, etc., since the method of treatment must vary according to the indications in the particular case, while a combination of methods is often necessary.

He has found that the use of radium needles gives better results in selected cases than the use of plaques or capsules. He describes in a general way the technic of the use of radium in needles, and by means of photographs describes some gratifying results.

SENEAR, Chicago.

EPITHELIOMA OF THE LOWER LIP. EVERETT S. LAIN, J. A. M. A. **75**: 1052 (Oct. 16) 1920.

As noted by others, the reports analyzed by Lain, obtained from a study of 122 cases, also show epithelioma of the lower lip to be far more common in outdoor workers, and most frequently seen in the side of the mouth in which a cigar or pipe is held. Early diagnosis and treatment of the lymph drainage of the lips will materially raise the percentage of cures. Neither surgery, radiotherapy nor any other one successful method of treatment should be used in all cases alike. Radium and the roentgen ray, singly or combined, give the most satisfactory results in a selected class of epithelioma of the lower lip.

WAUGH, Chicago.

A CASE OF CASTELLANI'S ACLADIOSIS. MENDELSON, Brit. M. J. **2**:3 (Oct.) 1920.

The author reports a case of acladiosis in a Chinese coolie working in Siam. Several ulcers resembling yaws were observed on the left leg below the knee. They were covered with a yellow scab which, when removed, showed a collection of thick creamy pus. The borders of these ulcers were clearly defined and surrounded with normal tissue. Cultures on glucose agar yielded an abundant growth and on microscopic examination a fungus showing all the characteristics of *acladium castellanii* was found. Large doses of mixed iodids produced rapid and satisfactory results.

OLIVER, Chicago.

EFFECT OF THE SUN'S LIGHT ON A SYPHILITIC ERUPTION. C. RASCH, Brit. J. Dermat. & Syph. **33**:56, 1921.

Rasch records an interesting observation made in the case of a young girl who exhibited a profuse papular syphilitic eruption; the eruption stopped at the border of that bared and pigmented portion of the skin of the back and chest corresponding to the cut of the dress. The skin of these parts was deeply pigmented, due to the fact that the patient spent two hours daily wheeling her mistress in the sun.

Rasch feels that the luminous or ultraviolet rays of the sun are responsible for the suppression of the eruption, since experience shows that heat rays, as is seen in the case of firemen and cooks, have exactly the opposite effect.

SENEAR, Chicago.

DIE PELLAGRA IM TRENTINO NACH DEM KRIEGE (PELLAGRA IN TRENTINO AFTER THE WAR). GUIDO DE PROBIZER, Dermat. Wchnschr. **71**:751 (Sept.) 1920.

The author calls attention to the rare incidence of pellagra in Trentino during the four years of the war in spite of the hunger, malnutrition and bad

hygienic condition of the people. He believes this decrease of the disease was due to the small consumption of corn on account of its high price and scarcity.

KETRON, Baltimore.

EINE NEUE METHODE DER GRAPHISCHEN DARTELLUNG VON HAUTVERÄNDERUNGEN. INBESONDERE DER SCHWIELEN-BILDUNGEN DER FLACHHAND (DERMATYPIE) (A NEW METHOD OF GRAPHIC PRESENTATION OF SKIN CHANGES. ESPECIALLY CALLUS FORMATION [DERMATYPE]). MORIZ OPPENHEIM, Arch. f. Dermat. u. Syph. **123**:709, 1916.

Oppenheim utilizes the printing ink method, which most of us who went through the identification card system of the army have already encountered, in order to get records of skin configurations. He claims, and the reproductions given bear him out, that good results are obtained with dry skin conditions, such as papules, nodules, scars, etc. For the palm of the hand callous formation may be recorded in this manner. The method will not, of course, replace photography or moulages.

GOODMAN, New York.

A PROPOS D'UN CAS DE BRANCHIOMES CUTANES BENINS (REGARDING A CASE OF BENIGN CUTANEOUS BRANCHIOMATA). J. DARIER, Ann. de dermat. et syph. **10**:433, 1920.

This report completes the author's previous article¹ on the subject. Following an operation, the author had the opportunity of examining sections from the fresh specimen. He found that the cells were nonciliated, and noted the existence of adenomatous tissue subjacent to the fistulae and communicating with them. No plausible new interpretation suggested itself.

PARKHURST, New York.

EIN FALL VON DERMATITIS DURCH SPARGELSAFT (A CASE OF DERMATITIS DUE TO ASPARAGUS. C. BRENNING, Dermat. Wchnschr. **71**:851 (Oct.) 1920.

The author reports the case of a patient who suddenly became sensitized to asparagus after having worked with it for eight years. A dermatitis was produced on the arms which after healing was experimentally reproduced by application of asparagus.

KETRON, Baltimore.

NAEVO-ENCEPHALOME (NEVO-ENCEPHALOMA). C. AUDRY, Ann. de dermat. et syph. **8-9**:369, 1920.

A child of 3 years presented two small tumors, one in the vertical region of the scalp near the bregma and to the right of the median line, the other in the frontal region over the right brow. Both were congenital.

The microscope showed them to be cutaneous tumors containing encephalic tissue, though they were not connected with the brain itself. Embryology is invoked in an attempt to explain their origin, but in the case of the vertical tumor the interpretation is difficult.

PARKHURST, New York.

1. Darier, J., and Halle, J.: Fistules branchiales multiples, Ann. de Dermat. et de Syph. **1**:1, 1920.

A STUDY OF THE SPINAL FLUID IN FIFTY-TWO CASES OF CONGENITAL SYPHILIS. LYLE B. KINGERY, J. A. M. A. **76**:12 (Jan. 1) 1921.

This is an interesting report in which a few case records are given. Emphasis is placed on the frequency with which cerebrospinal involvement is associated with early syphilis.

The importance of the routine lumbar puncture is again urged, not only because of its immediate value as a diagnostic procedure, but also on account of its influence on the ultimate prognosis in a given case.

WAUGH, Chicago.

LA REACTION A L'OR COLLOIDAL DU LIQUIDE CEPHALO-RACHIDIEN (THE COLLOIDAL GOLD REACTION IN THE SPINAL FLUID). A. PENSELLE, *Ann. de dermat. et syph.* **8-9**:375, 1920.

A review of the accepted technic and the interpretations of the reaction are given. It is considered valuable, especially when the other laboratory findings are negative.

PARKHURST, New York.

PEMPHIGUS FOLIACEUS UND OSTEOMALAZIE (PEMPHIGUS FOLIACEUS AND OSTEOMALACIA). WALTHER SCHULTZE, *Dermat. Wchnschr.* **71**:944 (Nov.) 1920.

The case reported is that of a woman 33 years of age, who had suffered for nine years with pemphigus vulgaris which had lately developed into the foliaceus type. While under treatment in the hospital she developed muscle atrophy and a kyphosis which became very noticeable. Bone changes were demonstrated by the roentgen ray.

KETRON, Baltimore.

ABSCCESS OF THE TONGUE. J. C. DALLENBACH, *Illinois M. J.* **38**:522 (Dec.) 1920.

This article contains a discussion of the acute and chronic infections of the tongue with the report of a case of acute abscess of this organ.

MICHAEL, Houston, Texas.

ALKOHOL UND GESCHLECHTSKRANKHEITEN (ALCOHOL AND VENEREAL DISEASE). VON NOTTHAFFT, *Arch. f. Dermat. u. Syph.* **123**:658, 1916.

Von Notthafft gives the results of his careful investigations concerning the relation between the first sexual adventure, the first attack of venereal disease, and alcohol in 187 men and three women. He is led to conclude that alcohol has not deserved the important place it has assumed in venereal disease and sexual offences that certain writers have been all too willing to give it.

GOODMAN, New York.

THE SYPHILIS CLINIC: ITS ORGANIZATION. EQUIPMENT AND PERSONNEL. HERMAN GOODMAN, *Boston M. & S. J.* **183**:667 (Dec. 9) 1920.

Goodman outlines the organization of a syphilis clinic under various headings, devoting attention to many details. He discusses its location, equipment,

personnel, record system, instructions to patient, and gives lists of supplies. He bespeaks the cooperation of the physicians in the community.

LANE, Boston.

SU DI UNA FORMA POCO COMUNE DI CATARATTA CONGENITA BILATERALE IN RAPPORTO A SIFILIDE EREDITARIA (A RARE FORM OF BILATERAL CONGENITAL CATARACT IN HEREDITARY SYPHILIS). S. BALDINO, *Rif. med.* **36**:833 (Sept. 11) 1920.

Double cataract, central and marginal in hereditary syphilis is of rare occurrence. The author reports a case in detail.

PARDO-CASTELLO, Havana.

TINEA CAPITIS—ROENTGEN-RAY TREATMENT. C. G. LANE, Boston M. & S. J. **183**:673 (Dec. 9) 1920.

This article is a review of the technic of the modern roentgen-ray treatment of tinea capitis, including standardization of apparatus, measuring of the scalp and its exposure, and after-care. Emphasis is placed on the necessity for attention to detail in the whole procedure.

LANE, Boston.

XERODERMA PIGMENTOSUM, PRESENTACION DE DOS CASOS (XERODERMA PIGMENTOSUM: REPORT OF TWO CASES). V. PARDO-CASTELLO, *Rev. méd. Cuba* **31**:429, 1920.

Pardo reports two extensive cases of this disease in two sisters, 10 and 7 years old. They had several epithelial growths and nevi on the face. The pigmentation covered practically the whole body. The author discusses the etiology and reviews the literature. The article is accompanied with four photographs.

PARDO-CASTELLO, Havana.

PULMONARY INFECTION BY SPOROTHRIX OF SCHENK. F. LE BLANC, *Illinois M. J.* **38**:516 (Dec.) 1920.

Two cases, clinically simulating tuberculosis of the lungs, were shown after repeated sputum examinations to be sporothrix infection. In each case a yellowish, firm, submucous granuloma, the size of a split pea, was present in the throat. These nodules were excised, but neither the mycelia nor the sporothrix proper was found in them.

MICHAEL, Houston, Texas.

CLINICAL NOTE: A CASE OF SO-CALLED "MULTIPLE HEMORRHAGIC SARCOMA" (KAPOSI). W. KNOWSLEY SIBLEY, *Brit. J. Dermat. & Syph.* **32**:331 (Nov.) 1920.

This case, the features of which are reported in detail, is of interest because the patient, a man aged 72 years, of English parentage, had never left the country, and because the primary lesion apparently occurred at the site of an injury to the back of the right hand.

SENEAR, Chicago.

DERMATOLOGIC ABSTRACTS

JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION

THE OFFSPRING OF PERSONS WITH INHERITED SYPHILIS.

SIDLER-HUGUENIN, Schweiz. med. Wchnschr. **51**:49 (Jan.) 1921.

Sidler-Huguenin has been examining the children of 250 persons who he knew were subject to inherited syphilis. This included 50 families, and 28 per cent of them were childless. He mentions further that among the 250 persons with inherited syphilis, only nine lived to be 60 years old. The male sexual organ seems to be injured more than the female by inherited syphilis, judging from the lesser number of children in the families in which the father was the parent that had inherited syphilis. He could not find any characteristic symptoms of inherited syphilis in the sixty-five children of the second generation except in one case, and this was not certain. The normal roentgen-ray findings and the negative Wassermann tests testify against syphilis even in this case. Persons with inherited syphilis can thus be reassured that their children will not feel the effects of it, although there is more probability of childlessness than under normal conditions.

ARE THERE MORE STRAINS THAN ONE OF SPIROCHAETA PALLIDA? Editorial, J. A. M. A. **76**:864 (March 26) 1921.

In 1894, Fournier¹ introduced the concept "parasyphilis," and his investigations and deductions, with those of Erb, have been considered as important contributions confirming the causal relation of syphilis to paresis and tabes. Although the term "parasyphilis" has fallen into disrepute, the definite linking of *Spirochaeta pallida* with the two diseases provided a large field for experimentation and speculation. Thus, the questions whether neurosyphilis is to be considered as a manifestation of a disease more commonly associated with lesions of other structures, or whether there are more strains than one of the spirochete, have attracted the attention of many scientists. What Fournier demonstrated by clinical methods Noguchi afterward confirmed by recovering the spirochete from the brain, subarachnoid fluid and blood of general paralytics.

After the establishment of the syphilitic origin of paresis and tabes, it was natural that the relative frequency of their occurrence in the history of the disease should be subject to scrutiny by syphilographers, and that investigation should be undertaken to account for the wide divergence in symptoms of a disease attributable to a common causative agent. In 1893, Morel-Lavalée² quoted the now well known case of the girl Marthe X, who in 1870 and 1871 infected five successive lovers with syphilis, each of them succumbing later to paresis. While this series may have had the significance of *post hoc* rather than *propter hoc*, it stimulated investigation to determine whether the exciting cause of syphilis in its many forms was a single organism or whether there were diverse strains of the responsible spirochete.

Up to the present, nothing absolutely definite has come out of these researches. In 1914, Nichols³ reported the results of a series of experiments relative to the localizing power of *Spirochaeta pallida* and suggested that

1. Fournier: Les affections parasyphilitiques. Paris, 1894.

2. Morel-Lavalée: Paralyse générale et syphilis. Rev. de méd. **13**:137-154, 1893.

3. Nichols, H. J.: Observations on the Pathology of Syphilis, J. A. M. A. **63**:466 (Aug. 8) 1914.

there were more strains than one of the organism. The same author⁴ later reported on experiments made with a strain of *Spirochaeta pallida* recovered from a patient with neurosyphilis, and in this report suggested the existence of different strains with varying invasive power and with individual characteristics. He cited the three forms of the spirochete classified by Noguchi, the thick, thin and medium, and stated that the one with which he worked belonged to the first type. "The question of the variation of strains of a pathogenic micro-organism is a complicated one," he says, "and calls for a consideration of variations in the host as well as in the parasite itself." In 1916, Reasoner⁵ reviewed the work of Neisser, Uhlenhuth and Mulzer, Steiner, Weygandt and Jacob, Noguchi and Nichols, and Wile, Zinsser and Hopkins, and further elaborated that done with a strain isolated by Nichols and Hough from a "neurorecidiv." From a number of experiments on rabbits, he concluded that it is possible to demonstrate satisfactorily fixed differences in various strains of syphilis as found in the rabbit; that it is possible to produce nervous involvement in the rabbit without actual intracranial inoculation; that no morphologic differences in the various strains were discovered, and that granting that there are different strains or types of syphilis differing in invasiveness or predilection for certain tissues, the individual resistance of the infected person must still be considered as a factor in the development of the disease.

Of the work undertaken on the continent along this line, that of Levaditi and Marie⁶ attracted wide attention. Their studies began in 1914, and were first reported on in 1919. Both are strongly of the opinion that there are two independent strains of *Spirochaeta pallida*, one of which they term the dermatropic and the other the neurotropic, in accordance with their selective action on body structures. In two instances, through accidental inoculation of investigators, they had opportunity to observe results in the human species. Among the significant facts brought out were the different selective affinity for the two so-called strains: the difference in the periods of incubation and, what seems particularly significant, the fact that an animal infected with one strain, while immune to subsequent inoculation with the same virus, has no acquired immunity to infection by the other strain. While they admit the possibility of the evolution of a special strain from a common source, by propagation in the nervous centers, they suggest that this evolution may give rise to a really new strain and that this strain may persist like a mendelian variant as such in place of reverting to its former characteristics; that a developed neurotropic spirochete will thereafter function as such rather than lapse again into a form which may embrace dermatropic attributes. As academic support of their theory, they cite the fact that immunity to any one of the relapsing fevers, African, European or American, does not safeguard the patient from an infection against the others, in spite of the morphologic resemblance of the spirilla and the similarity of the course of the disease which they produce. More recently, Pagniez⁷ reviewed this report, and remarks that we are coming more and more to the belief in the existence of different strains in the same micro-organisms, as evidenced by the tendency toward the use of polyvalent serums. To him virulence of the organism seems to be the great important factor, and he concludes that syphilis cannot long claim exemption to this law, and that even at the present time one would not be far wrong in differentiating strains in the virus of the disease.

4. Nichols, H. J.: J. Exper. Med. **19**:362, 1914.

5. Reasoner, M. A.: Some Phases of Experimental Syphilis. J.-A. M. A. **67**:1799 (Dec. 16) 1916.

6. Levaditi, C., and Marie, A.: Etude sur le treponème de la paralysie générale, Bulletin de l'Inst. Pasteur, November, 1919, p. 741.

7. Pagniez, P.: De la pluralité des germes syphilitiques, Presse méd. **28**: 266 (May 1) 1920.

Finally, Laumonier⁸ does not agree with Levaditi and Marie. He is inclined to believe that there is a difference in the host rather than in the organism itself, and that the variance in results may be accounted for on this ground rather than by any divergence in the strains of the spirochete itself. This side of the question is, of course, equally entitled to consideration. It is fundamental to the science of bacteriology to consider in any infection the virulence of the infecting organism and the resistance of the host. Further investigations of the various phases of syphilitic infection may possibly bring to light facts which will tend materially to betterment of our knowledge of the etiology of syphilitic manifestations and corresponding improvements in therapy.

8. Laumonier: Y-a-t-il plusieurs syphilis? *Gaz. d. hôp.*, Aug. 19 and 20, 1920, p. 1127.

Society Transactions

CHICAGO DERMATOLOGICAL SOCIETY

Annual Meeting, Jan. 19, 1921

WILLIAM ALLEN PUSEY, M.D., *Presiding*

LEPROSY.—Presented by Drs. STILLIANS and OLIVER.

The patient was a negress, a laundress, aged 28 years, born in the United States, who entered Cook County Hospital, Feb. 23, 1920. The present trouble began in February, 1919, as a dark red papule on the left side of the face at the level of the zygoma. Soon afterward papules appeared on the forehead and right cheek. Within six months the lesions had involved the entire face, including the lobes of the ears. Within the year the disease had involved the arms, hands and feet.

LEPROSY. Presented by Drs. STILLIANS and OLIVER.

A dye setter, aged 34 years, born in Serbia, who had been in this country for fourteen years, entered Cook County Hospital, Nov. 20, 1919. The present illness began in November, 1917, with general malaise, fever and chills. When he entered the hospital, he complained of a general nodular eruption involving the face, hands, legs and feet, swelling of the feet, numbness of the hands and feet, and loss of weight. At the time of presentation, he had improved considerably.

DISCUSSION

DR. STILLIANS said both patients had leprosy. They had received little treatment except sodium gynocardate A, administered intravenously and part of the time by mouth. The negress was born in Louisiana and had lived there until about a year ago.

DR. STOKES called attention to the fact that the leprosarium had just been opened in Louisiana, and that Dr. Denny was in charge.

DR. WILE said that in the case of a leper recently under observation at the University Hospital, who had a typical nodular type of the disease, it was found that all apparently normal skin taken anywhere on the body was loaded with lepra bacilli. He had removed several pieces of skin and sent one to Dr. Markley and one to Dr. Grindon, both of whom verified the findings.

CAPTAIN HAMILTON, R. M. C., said that they frequently saw leprosy in Australia among the Kanakas and Chinese.

DR. STOKES asked how many of the members had seen marked adenitis in leprosy. He had seen only one patient with large glands in the neck and axilla which had been removed as tuberculous. The pathologic picture was similar to that of caseating tuberculosis.

DR. QUINN said that the Serbian had been presented by him in Dr. Ormsby's clinic at Rush Medical College before he was sent by the health commissioner to the county hospital. At that time the man had large nodular lesions on the forehead and ulcers on the legs, also anesthetic macular lesions over the body. The roof of the mouth was involved with nodular ulcerations which looked like syphilis, so much so that the man had received eight injections of arsphenamin without any results. At present the case appeared entirely different, and there had been great improvement. He had started him on gynocardate of sodium, and the patient had taken this up to about 60 drops, with much benefit. He had been working in the carpet department at the county hospital for the last six months.

DR. GUY stated that he had seen one case of leprosy in which there had been considerable adenitis, but they found the patient had syphilis as well. Dr. Guy wished to know whether the members considered it absolutely essential in these cases to identify Hansen's bacillus. He had the impression that certain other diseases clinically simulated leprosy closely, and that they could not be diagnosed as leprosy unless Hansen's bacillus was identified.

DR. STILLIANS stated that a patient with nodular leprosy seen several years ago had had distinct adenitis in the groins and axillae, especially during his febrile attacks. He did not remember about the cervical glands. He was interested in the nail lesions in the case of the negress because the textbooks said that they were rare in the nodular cases.

The dosage of gynocardate administered intravenously had been increased to 6 c.c., with only moderate reaction in the case of the man. The woman could not stand such high dosage.

DR. PUSEY, replying to Dr. Guy, said that he had recently received a communication from a well-known leprologist who said that they did make the diagnosis of leprosy without finding the bacillus, in some instances. Dr. Pusey did not understand why this was necessary.

LUPUS ERYTHEMATOSUS. Presented by DR. WELFELD.

The patient was a man, aged 32 years, who had never suffered from any nervous illness nor had any skin disease. The present condition of the lip began as a crack on the left side, two years ago. He had tried various remedies, without effect, for months. He was treated at the Cook County Hospital with roentgen therapy for about six weeks, with no result. The Wassermann reaction a year ago was negative, but despite that he was given eight injections of mercurial oil at weekly intervals, which had had no effect on the lesions. Examination of a piece of excised tissue showed no malignancy, but chronic superficial inflammatory changes. The changes in the lip were progressive, and at the time of presentation, practically the entire vermilion border was affected by an erosion while the cutaneous surface near it showed atrophied rounded areas, the borders of which presented some desquamation.

DISCUSSION

DR. GRINDON asked whether there was ulceration prior to the use of roentgen therapy.

DR. BUTLER thought that some of the lesions suggested a lupus erythematosus, but the clinical qualities had been so changed by therapy that on glancing at it one could not help thinking of cheilitis exfoliativa.

DR. LIEBERTHAL said that if only the vermillion border of this case were seen in its present condition, there could be a suspicion of its being one of cheilitis exfoliativa. But the changes of the skin next to the vermillion border stamped it as one of lupus erythematosus.

ERYTHRODERMIE PITYRIASIQUE. Presented by DR. R. S. WEISS for DR. ENGMAN.

A man, aged 55 years, a clerk in a railroad office, had a disorder which began in 1905 as a few spots over the sternum and generally spread to other parts. Changes in the weather caused a mild burning and itching of the affected areas. When a plaque appeared, it never disappeared. The Wassermann reaction was negative. There was a mild hypertension. The urine showed a trace of albumin.

DISCUSSION

DR. SENEAR thought that the diagnosis offered was the proper one.

DR. IRVINE agreed with the diagnosis, but thought the lesions on the lower extremities were rather more abundant than was usually the case in this disorder. They were more likely to predominate on the trunk. In his opinion the thickening of the skin was due to the fact that it was the lower extremities that were involved. He believed that almost any lesions on the legs were accompanied by a certain amount of edema, making the skin appear thickened.

DR. GRINDON thought the diagnosis was correct, but sounded a note of warning as to these cases. It had been his misfortune to see a case in which he made a diagnosis of erythrodermie pityriasique of the pityriasis rosea-like type. The patient failed to respond to any treatment and ultimately died of mycosis fungoides. The condition may be counterfeited by the premycotic lesions of mycosis fungoides. Rarely, as in three of Crocker's cases, itching is absent, thus further obscuring the diagnosis.

DR. COLE thought the case interesting, and believed it was one of the two disorders.

DR. FOERSTER said the discussion brought to mind a patient in whom the premycotic stage of mycosis fungoides had lasted for about twenty-two years. That patient, however, had distinct itching, which Dr. Foerster believes is a point of importance in the differentiation of these cases. The diagnosis was made correctly by the late Dr. Hyde, after the diagnosis of Brocq's disease had been made by various experts in Europe. In Dr. Engman's patient, he favored the diagnosis of the large plaque type of Brocq's erythrodermia.

DR. PUSEY said he always disliked the diagnosis of "premycotic stage of mycosis fungoides" in doubtful cases because it was a sort of refuge in perplexity. To his mind the absence of itching in a case suggesting the premycotic stage of mycosis fungoides made it difficult to make a diagnosis of mycosis fungoides.

DR. STOKES said that a year ago he saw a physician with a general erythroderma and the early lesions of mycosis fungoides, but he could not get the patient to admit that the lesions had ever itched. He said the skin felt dry and drawn, but there was no itching, although the erythroderma had existed for eighteen years. Recent reports indicated that the patient was evidently progressing. This was one patient—a reasonably good observer—who said his lesions had never itched.

DR. WEISS stated that itching had not been a feature of this man's case, although he at times experienced slight itching when he became warm. This fact was considered in the differential diagnosis.

PITYRIASIS RUBRA PILARIS. Presented by DR. OLIVER.

A boy, 12 years of age, had had lesions for four years which began with the development of small, hard, horny papules on the dorsum of the feet. Later the palms and soles became hyperkeratotic. When first seen July 28, 1920, small, hard, horny, acuminate papules were seen on the dorsa of the feet; several were also noted on the dorsal surfaces of the fingers, situated at the orifice of the hair follicles. The palms and soles were very hyperkeratotic, and there were scaling infiltrated patches present on the elbows and the knees. The boy was a well-nourished, healthy lad, and there were no subjective symptoms.

DISCUSSION

DR. GRINDON considered the diagnosis of pityriasis rubra pilaris absolutely clear. On the dorsa of the feet were typical patches. On the knee there was the cross-hatching typical of old patches. There was not the amount of scaling that one expected to see, but this might be due to treatment. The most significant thing to him was that each popliteal space was bounded on each side by a linear patch, in places merely showing infiltration, in other places papules with little central scales, if not plugs. In his opinion this appearance was typical; while it is not present in all cases, when it is seen it is like a signature, the parallel streaks running down each hamstring. The disease presents different appearances in different grades and stages of severity, but is not necessarily severe, there being many mild cases, as was so well brought out in the classic description by Besnier and Doyon, in their annotations to Kaposi's treatise. Some of those present might remember photographs published in 1884 by Dr. George Henry Fox, and a picture labeled "Lichen Ruber" showing patches covered with a dense white scale in which these streaks over the hamstrings were beautifully shown.

DR. BUTLER considered the case of unusual interest, but could hardly concur in the diagnosis. While it is true that the hyperkeratotic palms and plantars are usually found, there was total absence of the scaling which was almost invariably present; there was no follicular hyperkeratosis and the phalanges showed no keratotic plugs.

DR. WILE said that after Dr. Grindon's adequate exposition of the varieties of pityriasis rubra he was a little more loath to agree with Dr. Butler than he was before, but he still had to be convinced that the case was one of pityriasis rubra pilaris. He thought perhaps this was due to the fact that he had seen fewer cases than Dr. Grindon, and most of them were generalized. Granting the different pictures, notably the symmetry and also the streaking that Dr. Grindon called attention to, he was impressed, as was Dr. Butler, with the complete absence of any scaling, with the fact that in the four years' duration the disease had not progressed, and that it was apruritic. Most of the cases he had seen had been extremely itchy, particularly in the generalized cases. He believed the case might be considered as belonging in the group of congenital keratosis of the palms and soles, or the so-called "keratosis palmaris et plantaris," either congenital or occurring shortly after birth. He

had noticed a few follicular plugs on the instep, but one usually looked for them on the abdomen, on the back of the thighs and phalanges. He considered it a keratoderma of the palms and soles.

DR. ZEISLER stated that he had had a considerable number of cases of pityriasis rubra pilaris under observation in the last few years. In one family four members were affected—the father and three children. The disease in the children was of a much milder type. Regarding the presence of scaling, Dr. Zeisler thought this was easily modified by bathing. The distribution in Dr. Oliver's case corresponded exactly to the cases he had observed; the symmetrical involvement of the knees and palms and soles was typical. There were follicular hyperkeratotic lesions around the ankles, and he believed it was definitely a case of pityriasis rubra pilaris.

DR. WILE was of the opinion that the congenital history in Dr. Zeisler's cases would bring them into the congenital group of dystrophies.

DR. COLE recalled having seen one of Dr. Zeisler's patients, and in that case there was no pruritus. He did not think it was necessary to have pruritus to make a diagnosis of this condition.

DR. CREGOR thought there was no question about the diagnosis of pityriasis rubra pilaris. He had noticed a hyperkeratotic follicular process about the knee and instep, and would not have to draw on his imagination to recognize some lesions of the same process on the dorsal surface of the hands.

DR. MARKLEY thought if this was a case of pityriasis rubra pilaris, the disease was more common than he had been led to believe. He had seen several cases in which plantar and palmar hyperkeratosis had occurred in addition to other situations in which friction was apt to take place and similar involvement of the popliteal spaces on one side or the other. Pityriasis rubra pilaris had always in his experience been accompanied by some scaling or other involvement of the scalp, which so far as he could see was missing in this case. He also did not see any involvement of the dorsal surfaces of the phalanges. As to the condition about the ankles and insteps, Dr. Markley thought this might occur in any one who wore ill-fitting shoes, and particularly in a person with a tendency to hyperkeratosis. If this was a congenital tendency this condition might develop with even slight degree of friction. Dr. Markley was in accord with Dr. Wile in regard to the case.

DR. WAUGH recalled that during the years he was associated with Dr. Ormsby he saw several cases similar to this one. In one case the only lesions present were on the palms and soles, and resembled plantar keratoses; a year later the child was practically covered with typical lesions of pityriasis rubra pilaris.

DR. OLIVER stated that before he saw the patient he had been treated for four years for psoriasis. There was so much scaling and infiltration on the elbows and knees at that time that the diagnosis of psoriasis had been made.

ERYTHEMA MULTIFORME OF THE BUCCAL AND LINGUAL
MUCOUS MEMBRANES, WITHOUT CUTANEOUS MANIFESTA-
TIONS. Presented by DR. BUTLER.

A boy, aged 16 years, who had always been in excellent health, in October, 1918, suffered from an attack of erythema multiforme with erythema iris lesions on the dorsal surfaces of the hands and feet; the buccal and lingual mucous membranes were later involved, with severe denuded areas. About one

year later he had a similar attack, and he has had two subsequent attacks at five month intervals. In all of these attacks the lesions were of the erythema iris type. The present or fifth attack began fifteen days before the date of presentation. The cutaneous surfaces were not involved. The attacks are not preceded or accompanied by constitutional disturbances. At the present time the buccal and lingual mucous membranes are covered with typical erythema multiforme lesions.

DISCUSSION

DR. ZEISLER stated that he had seen several of these cases recently. Two of the patients had been at the county hospital, one with a peritonsillar abscess and the typical erythema multiforme lesions of the skin and mucous membranes. He had seen a third patient with mucous membrane involvement in the wards at Wesley Hospital; this case had been diagnosed as syphilis. He thought it was possible to make the diagnosis from the mouth lesions, particularly the lesion on the lip. It was unusual to find a purely mucous membrane involvement.

DR. HAASE asked whether the usual erythema multiforme lesions had appeared in all the previous attacks. He was under the impression that the mouth lesions had appeared without the appearance of lesions on the skin, and the thought suggested itself that the erythema multiforme lesions might have been secondary to some pathologic condition in the mouth. If they had been present in previous attacks, he agreed with the diagnosis of erythema multiforme.

DR. PUSEY considered the case interesting and thought that with the pictures shown of the hand lesions in previous attacks the diagnosis was above question, but in his experience such a case was unique. He had seen no other case of erythema multiforme of the mouth that was unaccompanied by skin lesions.

DR. BUTLER stated that in all the previous attacks the lesions had been of the erythema iris type. This was the fifth attack, and no cutaneous lesions had developed.

LICHEN ATROPHICUS. Presented by DR. WAUGH.

The patient was a woman, aged 40 years, whose disorder had been present for fifteen months. Whitish atrophic patches had appeared on each breast and some small, split-pea-sized, discrete lesions were present. When the lesions first appeared, they were accompanied by moderate itching. A few lesions had appeared on the flexor surfaces of the wrists which left a brownish pigmentation when they disappeared.

DISCUSSION

DR. MICHELSON was impressed with the fact that the lesions began with atrophy, and the bullae and vesicles were secondary. He believed the case was one of macular atrophy.

DR. BUTLER called attention to the fact that the lesions were ringed, and as involution took place scarring occurred. When he first saw the patient he thought the condition was lupus erythematosus, but later changed his mind and believed it was lichen atrophicus.

DR. MITCHELL thought it was lichen planus atrophicus with intertriginous dermatitis in a fat woman whose breasts were in constant apposition.

DR. WAUGH said that some of the areas were unduly infiltrated and inflamed owing to the pendulous breast, moisture and heat. The patient also had a patch on the abdomen, which was likewise reddened. Some of the patches were not entirely white when they first appeared, and others were quite white, like those on the breasts.

LUPUS ERYTHEMATOSUS AND PERNIO. Presented by DR. WAUGH.

The patient was a young man, aged 19 years, whose disorder had been present for two years. The first symptom was a bluish red appearance of the lobes of the ears and the hands. Itching and burning sensations, especially of the ears, were noticed, together with an erythematous area, over the right side of the nose which had persisted. There was also a dime-sized erythematous, slightly infiltrated spot on the left cheek, and a few erythematous papular lesions were present on the dorsal surface of the hands and fingers. Scaling areas were present on the lobes of the ears, but at no time had vesicles appeared. The hands were cold and the palms moist from perspiration. There were no scars. The disorder practically disappears in the summer and recurs with the onset of cold weather.

DISCUSSION

DR. SENEAR felt that the lesions on the ears and nose were those of lupus erythematosus, that the condition of the hands was a pernio-like affair which was sometimes seen in that condition, and that this furnished a basis for the development of a papuloneurotic tuberculid. He offered a diagnosis of lupus erythematosus and papulotuberculid.

DR. WAUGH said that the history was typical of pernio, and the condition on the nose and ears seemed to be a superadded lupus erythematosus. Several cases of lupus erythematosus developing in typical pernio had been reported.

ARSENICAL HYPERKERATOSES AND PIGMENTATION. Presented by DR. WAUGH.

The patient was a boy aged 9 years, whose hands and feet were practically covered with hyperkeratoses. A dusky brownish pigmentation of the skin was present over most of the body, but was exaggerated on the trunk. He had been given Fowler's solution two years previously for chorea, in a dosage of 5 drops after meals, with instructions to increase the dosage to 10 drops, or a total of 30 drops daily.

DISCUSSION

DR. WAUGH thought an interesting feature of the case was that as long as the patient took 30 drops of Fowler's solution a day, it held the chorea in check, and that as soon as the administration of the solution was stopped the chorea appeared. He had found the teeth and tonsils in bad condition, and these were being cared for, as many cases of chorea clearing up rapidly after focal infection was eradicated were reported.

CAPTAIN HAMILTON cited the case of a woman (reported by him in the *British Medical Journal*, January, 1921) who had taken arsenic for thirty-five years and who came to the hospital with an epithelioma on the arm. The

interesting feature of the case was that they obtained arsenic by the Marsh test from the skin, the hair and the nails, showing that she was saturated with the drug. A pathologic examination of the section removed from the tumor showed it to be epithelioma.

A CASE FOR DIAGNOSIS. Presented by DR. STILLIANS.

The patient was a man, aged 24 years, a chauffeur. The disease had begun in 1916 as a sycosis and was confined to the bearded region until August, 1919, when a folliculitis appeared in the groins. Eczematoid dermatitis began on both wrists in January, 1920, and since that time the lesions on the groin had spread down the thighs. The scalp was involved early, with the bearded region. It itched intensely at times. Ointments had little influence, but the condition yielded to roentgen therapy. Both the Wassermann reaction and cultures were negative.

DISCUSSION

DR. LIEBERTHAL was of the opinion that the whole condition was a sycosis.

DR. GRINDON was much interested in the case. While it might be a sycosis, he did not feel certain about it. About the shoulders and the upper part of the back in the neighborhood of the axillae there were a number of closely grouped papules that were hard, some containing minute plugs—possibly scales rather than plugs. About the abdomen there were areas in which there was a distinct nutmeg grater-like feel, making one think, as far as those areas were concerned, of pityriasis rubra pilaris. Some of the areas on the chest, the general distribution, and the appearance of some of the lesions made one think of a mild case of Darier's disease. Dr. Grindon remained in doubt as to what the condition might be, although he admitted that Dr. Lieberthal's diagnosis might be correct.

DR. COLE was inclined to classify the condition as seborrheic dermatitis, accompanied by an infection. He thought this would account for the findings in the scalp, between the shoulder blades, under the arms and about the groins.

DR. ZEISLER said that the patient was under observation in their office a year or so ago, and at that time there were no patches on the body, but there were patches of seborrheic eczema on the bearded region and scalp.

DR. STILLIANS stated that when the patient first came to him he considered the disorder a sycosis, and when the case was presented to the Society the members agreed with him. The lesions on the chest were recent; there were none on the back to correspond and none on the nose. The lesions on the scalp had never extended beyond the hair line, and the ears had never been greatly involved. He believed the case had started as folliculitis. Histologic examination of sections showed an inflammatory infiltrate around the hair follicles. In his opinion it was a follicular infection in a man of low resistance, who was subjected to other infections as well. Later there was a sensitization of the skin and consequent eczematoid dermatitis.

DR. WEISS thought in view of Dr. Zeisler's remarks that Dr. Stillians' diagnosis of secondary eczematoid dermatitis of Engman was probably correct. Every one knew that pus in any part of the body might produce these lesions all over the surface of the skin. If the man had a sycosis previously there was no reason why it should not produce a secondary eczematoid dermatitis.

A CASE FOR DIAGNOSIS. Presented by DR. WAUGH.

The patient was a boy, aged 14 years, whose disorder had been present for five weeks. The lesions consisted of deep ulcers, small coin sized and dark red, with slight discharge and little pain, situated on and above the ankles. There were also a few split-pea-sized scars and pigmented spots on the forearms and legs below the knees from former lesions. There was pronounced adenopathy of the cervical glands. The Wassermann reaction was negative.

DISCUSSION

DR. WILE thought the case was one of ecthyma.

DR. STILLIANS called attention to the raised border and rather excavated edges, and said the case impressed him like those he had seen of diphtheria of the skin and a case at the county hospital with a deep necrosis at the center and a distribution like that of erythema multiforme. He had always thought these cases were due to local infection of the skin by blood borne organisms.

DR. BUTLER believed no one could consider the case without thinking of factitious dermatitis. The ulcers were such as he had never seen produced by pus infection, and it looked to him like a normal skin which had been insulted by chemicals.

DR. GUY thought possibly it was an infection by one of the higher bacteria, the *Sporothrix* or *Nocardia*, on account of the gumma-like lesions, with softening, ulcerations, and comparatively little pain. This was only a tentative diagnosis and could not be proved without further study of the case.

DR. GRINDON had seen lesions just like these due to "chigger" bites which were scratched and infected and then scratched some more, until such lesions developed. If the condition was seen in an older patient one would think of epithelioma, for the lesions had a built up border and central ulceration. He believed this case to be nothing but a much scratched ecthyma.

DR. WAUGH did not think the case was an ordinary pus infection. To him the case appeared suggestive of a *Streptothrix* infection. The family history was negative as to syphilis; the boy showed no signs of that infection, and the Wassermann reaction was negative.

A CASE FOR DIAGNOSIS. Presented by DR. WAUGH.

The patient was a child, aged 8 months, who at birth was normal in development and appearance, with the exception of an unusual coating over the surface of the body; within two days this had dried and contracted, producing ectropion and inability to close the mouth. It resembled a collodion coating over the entire surface of the body. Exfoliation began in a few days, leaving a smooth, reddened surface. Soon after the skin would again begin to exfoliate and later become smooth. This process had occurred five times. The face, legs, buttocks and parts of the arms had been perfectly smooth and normal in appearance for two months. The scaling at times had been ichthyotic in appearance. The child appeared to be normal when presented, and was gaining weight.

(This patient was shown first at the May, 1920, meeting of the Society, and again at the October meeting, and a report of the case was published in the Society Proceedings, ARCH. DERMAT. & SYPH., January, 1921, p. 96.)

DISCUSSION

DR. ORMSBY said he saw the child the first time it was shown, at which time it had the remains of the collodion-like covering which it had at birth. His impression was that the case belonged to the small group of cases characterized by the persistence of the epitrichial layer after birth. These patients either died within a short time, or developed ichthyosis, and had formerly been reported as congenital ichthyosis. Dr. Ormsby presented a patient with this kind of a case before the Society about fifteen years ago, but that child died of pneumonia in about two weeks. Another patient was presented by Dr. Sherrill in New York, and at the time of the report the condition was three months old and thriving. Dr. Waugh's patient would evidently survive and could therefore be studied further.

DR. PUSEY thought the case was a typical one of persistence of the epitrichial layer described by Bowen.

DR. GRINDON thought it was necessary to distinguish between true ichthyosis and the condition generally called congenital ichthyosis, established as long ago as 1864 by Lebert as a distinct morbid entity under the name of hyperkeratosis congenita. True ichthyosis is not congenital but usually develops during the second year of life. So-called congenital ichthyosis, of which harlequin fetus is an exaggerated example, he believed should be differentiated as hyperkeratosis congenita.

DR. WAUGH had been much interested in looking up the literature, and expressed his thanks to Dr. Ormsby for first suggesting the diagnosis. He believed the case should not be classed in the ichthyosis group. The child was apparently recovering, and the skin was clearing up gradually. After about the fifth exfoliation of the entire skin, the arms, legs and face had become perfectly smooth and at present were normal, but the body still had ichthyotic patches. The case was of unusual interest because the patient had lived longer than any other on record.

CARCINOMA OF THE TONGUE. Presented by DR. SIMPSON.

This patient was presented to illustrate the method of inserting bare emanation ampules into the tongue. An instrument which Dr. Simpson has devised for this purpose was also exhibited. The instrument consists of a needle and plunger to which a handle is attached, and works in a manner similar to an ordinary Record syringe. By pressing the handle of the syringe, the small glass emanation apparatus is ejected from the end of the needle. The emanation ampule is allowed to stay in the tissues until its complete decay or until it sloughs out. It has been found that the ampules are harmless, even though they remain indefinitely in the tissues. Distinct improvement follows the insertion of the ampules into the carcinoma in the side of the tongue.

A total of 12 mc. had been inserted into the carcinoma in this case.

ONYCHOMYCOSIS. Presented by DR. WAUGH.

The patient was a woman who had had the disorder for several years. Most of the nails of the fingers and toes were involved. The nails were discolored, broken off and ragged in appearance, and much deformed.

DISCUSSION

DR. WAUGH said the case was one of onychomycosis and the *Trycophyton* fungus had been demonstrated.

DR. WILE said that he had recently had a case of onychomycosis for which Dr. Foerster had suggested a good treatment, in the face of failure on Dr. Wile's part and that of many others. The patient was a young lady who had been treated for psoriasis of the nails for about a year. After the mycelium was recovered from the scrapings of the nail she was treated by the textbook remedies and others, but Dr. Foerster suggested the use of nascent sulphur. The nails were first immersed in a 12 per cent. solution of sodium hyposulphite and then in a 2 per cent. solution of acetic acid, the treatment being used twice a day. Shortly after the treatment was instituted, he was impressed with the improvement of the nails and the great difficulty in demonstrating parasites. There was complete recovery in an incredibly short time.

DR. McEWEN said that he had used this treatment in ringworm of the scalp and found it satisfactory. He had estimated the percentage of each solution that would approximately neutralize and found that about 12 per cent. of sodium thiosulphate would neutralize 6 per cent. of dilute acetic acid.

RODENT ULCER OF THE FOREHEAD. Presented by DR. ZEISLER.

The patient was a man, aged 40 years, whose disorder had been present for seven years. It involved the deeper tissues and had failed to respond to the treatment with roentgen rays and radium which had been instituted at different periods. The case was presented for therapeutic suggestions.

DISCUSSION

DR. GRINDON asked whether the Kromayer lamp had been used.

DR. PUSEY considered the Kromayer lamp ineffectual in cases of this type.

DR. AUNER said his observation as well as experience had been that these cases resisted treatment because it was not adequate. In his opinion, the patients treated by radium received too little treatment. In his experience the so-called massive dose treatment made these cases respond favorably. It produced a terrific dermatitis, but this subsided and in from four to six weeks there was complete healing and a good cosmetic result. He had found that epitheliomas in the temporal region yielded nicely to radium therapy.

A CASE FOR DIAGNOSIS. Presented by DRs. ORMSBY and MITCHELL.

The patient was a woman, aged 64 years, who presented many subcutaneous abscesses and sinuses situated chiefly on the neck and upper portion of the chest. The disorder began as a swelling in the glands of the neck. Surgical procedure was employed, but new abscesses constantly formed and appeared in new situations. The case was carefully studied by early observers of the patient. The blood and spinal fluid were examined with negative findings. The bones were skiagraphed and the chest thoroughly studied, also with negative results. All cultures made from pus were negative. Each new lesion began as a deep swelling which gradually enlarged, softened and finally ruptured, discharging thick purulent material.

On examination the discharging sinuses were seen extending over both sides of the neck and down over the sternum; irregular scar formations were present and several soft swellings. During the nine months the patient had been under observation, all cultural work had been negative and the therapeutic measures employed, which included radiotherapy and potassium iodid, had produced no appreciable effect on the progress of the disorder.

DISCUSSION

DR. GRINDON asked whether a roentgenogram of the chest had been made.

DR. WILE thought that if one saw the case in a far younger person his first impression would be that it was tuberculosis. Perhaps one was too hasty in arriving at an opinion regarding tuberculosis as beginning in early life or adolescence. That particular point was brought out in the case of a woman who developed lupus erythematosus in the forty-fifth year. He did not believe a case of this kind allowed many possibilities. Infectious granuloma was suggested; the case did not look like syphilis, and one only had to deal with some obscure form of mycelial infection. He believed the condition was an unusual case of tuberculosis.

CAPTAIN HAMILTON said he saw a similar case in a boy and it proved to be actinomycosis. There was no demonstrable tuberculosis in the patient.

SARCOID (DARIER-ROUSSY TYPE) WITH PULMONARY INFILTRATION. Presented by DR. STOKES.

The patient was a woman, aged 28 years, whose disorder had been present for eight years, with gradual extension. The cutaneous lesions consisted of a bluish infiltration of the tip of the nose and a plaque on the left cheek suggesting lupus pernio. On the outer aspects of both upper arms were deep brownish infiltrations showing no distinctive configuration, practically flush with the skin and on diascopic pressure showing minute translucent nodules. There were scattered pea-sized indurations in the skin of the forearm, one toe was involved and there was a marked thickening of the approximal phalanges of the index fingers and thumbs. A diffuse pulmonary infiltration was present suggesting miliary tuberculosis more marked about the hilus of the lung; the axillary and epitrochlear glands also showed infiltration. Roentgen examination showed bone changes in the phalanges similar to those of fibrocystic disease. The case was diagnosed by a general pathologist as noncaseating tuberculosis. Biopsy material from the left epitrochlear gland and the lesion on the left arm was shown. The patient had had three attacks of pneumonia, one in childhood, one at 12 years of age and one following influenza two years ago. There was clubbing of the fingers, presumably secondary to the pulmonary condition. There was slight dyspnea on exertion. The liver and spleen were not palpable. The pulse, temperature and blood pressure were normal. The leukocyte count was 6,900; polymorphonuclears, 67.5 per cent.; neutrophils, 67.5 per cent.; small lymphocytes, 15 per cent.; eosinophils, 3 per cent. The von Pirquet test had twice been negative. Cultures of the epitrochlear gland yielded a diphtheroid organism. The Wassermann reaction was negative.

Before entering the Mayo Clinic, the patient had received from twelve to fifteen injections of arsphenamin with slight improvement; the Alpine sun lamp had been used for six weeks, without effect; she had received roentgen

therapy to the thumb and index fingers six years ago—about fifty treatments; potassium iodid, 30 minims three times a day for three months, had made the lesion worse. No vaccines or hypodermic injections had been administered until recently. While under observation at the Mayo Clinic she had received about forty injections of sodium cacodylate in $1\frac{1}{2}$ to 3 grain doses, three to four times a week, with practically no effect. Three intravenous injections of 5,000,000 bacteria each of a vaccine made from diphtheroid organism cultivated from the lymph gland had been administered without definite reaction, although following the first injection there was a suggestion of a focal flare-up in the arm lesions and a sensation of tightness and constriction in the chest. Suggestions as to therapy were desired.

DISCUSSION

DR. ORMSBY said that the patient who was shown about a year ago had a disorder similar to this which was of a mixed type with lesions on the face, arms, forearms and hands. This case had been well worked up by one of his associates, Dr. Finnerud, and he thought it would be interesting to have Dr. Finnerud tell about the findings since the cases were so much alike.

DR. FINNERUD stated that the case was like Dr. Stokes' in practically all the essentials. There was no adenopathy, and a most careful search for tubercle bacilli had proved negative. The bone changes in the two cases were about the same, and these were thought by Dr. Phemister to be due largely to a necrosis from pressure. The medullary substance was probably not affected primarily, and looked identically like that in the case shown by Dr. Stokes. Arsenic and roentgen therapy had been of little value, and there was practically no improvement.

DR. ORMSBY thought that as sarcoid had been the topic of so much discussion before the Society it might be of some interest to discuss the case he had shown at this meeting in connection with the others. This case was of the nodular and plaque type and the patient had lesions on the face. The patient had had lupus erythematosus for twenty-three years, and developed sarcoid in the lesions of lupus. The diagnosis of sarcoid in this case was made by Arndt in 1914, and arsenic was suggested for treatment. The arsenic treatment was used in this case for several months, and the patient recovered entirely. About four months ago, in the autumn of 1920, she developed a new lesion, and they again instituted arsenic and radiotherapy.

Another patient, who had been shown before the Society two or three times with lesions on the face, had since developed them on the hands and feet. This case was of the deep-seated type, and the patient had become worse in spite of everything that could be done. The face was almost a solid mass of nodules, the eyes almost closed, and the patient was in a pitiable condition.

Some patients had been presented whose condition had been cleared up by arsenic. At one time Dr. Harris showed a patient who he said had not improved under arsenic therapy, but when this treatment was persisted in for a longer period she did improve. Arsenic was the only drug that seemed to have any effect. Dr. Finnerud had been disappointed in the case he studied for he was sure they would be able to demonstrate the tubercle bacillus, but there was a negative reaction to all tests. As the case was typical and so recognized by all who saw it, and as the histology was similar to that

commonly seen in tuberculosis, it seemed promising for proving its tuberculous origin, but after working for a year they were unable to demonstrate tuberculosis by cultural or animal experimental or serologic tests.

DR. HAASE thought the case was exceedingly interesting in connection with the work done by Dr. Rosenow, who had obtained pure cultures of diphtheroid bacillus from the glands, but Dr. Stokes assured him that it was cultivated in a number of tubes. Dr. Haase suggested that intradermal injections of diphtheroid bacillus be tried.

DR. COLE said that he thought the diphtheroid bacillus had been overworked. It was always found on the normal skin, and made a culture that looked much like that of a streptococcus on ordinary medium. If there was any skin infection, it was the easiest thing in the world for the diphtheroid bacillus to be carried into the lymphatic system and into the glands. It had been found in numerous cases of Hodgkin's disease and of skin diseases, and it was a question in his mind whether finding the diphtheroid bacillus meant very much. His mind was open for conviction.

DR. STOKES said they did not intend to offer the diphtheroid bacillus as the etiologic factor. Shortly after this patient entered the clinic another patient had died who had presented much the same findings, without the cutaneous lesions, but with extensive visceral lesions. The glandular picture was not that of Hodgkin's disease, and the pathologists had called it non-caseating tuberculosis. This girl's blood count was interesting in that the large percentage of polymorphonuclear neutrophils was unusual. In reviewing the literature Dr. Stokes could find no evidence that any one had ever been able to secure a culture of anything direct or by animal inoculation. The case could not be regarded as tuberculosis in the restricted sense. It might be thought of, perhaps, as a connecting link between tuberculosis and the lymphogranulomas.

A CASE FOR DIAGNOSIS. Presented by DR. SENEAR.

The patient was a child, aged 7½ years. The eruption began suddenly when she awoke one day and complained of itching. There was a lesion on the left side of the chest. The eruption was bright red and vesicular.

DISCUSSION

DR. SENEAR stated that he saw the patient for the first time the day before presentation. He had with him Dr. Cepelka who, having just returned from Prague, characterized it as a typical case of herpes maculosus tonsurans of the erysipeloid type. The picture on the chest was a vesicular eruption with lesions of a crystalline type, while there was present on the side of the chest a single lesion of the pityriasis rosea type, making a complicated picture. There was nothing in the history that suggested an external or internal cause. At the last meeting of the Society there was considerable discussion of the various types of lesions which might be present in pityriasis rosea—the wide divergence from the ringed lesions with the fawn colored center, and the question as to whether the fine punctate lesions in the case then shown by Dr. Zeisler were really part of the pityriasis rosea. This case was presented because of the presence of the primary lesion of pityriasis rosea and the generalized eruption which did not conform to the typical picture but which Dr. Cepelka stated was herpes maculosus tonsurans.

DR. GRINDON asked which was present first. Basing an opinion on the present appearance, he considered it an erythema of toxic origin, with at one point a pityriasis rosea-like desquamation which he thought would rapidly spread over the whole surface.

DR. SENEAR said that no patch was noticed until the generalized eruption appeared.

MORPHEA. Presented by DR. ORMSBY.

A description of this case appeared in the ARCHIVES OF DERMATOLOGY AND SYPHILOLOGY.

DISCUSSION

DR. ORMSBY stated that this patient's case was recorded about sixteen years ago when she presented typical lesions over the upper part of the shoulders on the posterior surface of lichen planus atrophicus et sclerosis (Hallopeau). At that time cases of guttate morphea were included in the report, and the distinguishing features both clinically and histologically were brought out. Under radiotherapy the disorder cleared up. Three years ago, or thirteen years later, this patient developed on the abdomen a large patch of typical morphea, not the guttate form. The patient was shown on account of an interesting coincidence as there could be no connection between the original and the present disorder.

SARCOID. Presented by DR. ORMSBY.

This patient was presented in 1914. The eruption entirely cleared with the administration of arsenic. Recently one nodule reappeared.

DERMATITIS MEDICAMENTOSA RESEMBLING VARIOLA. Presented by DRS. ORMSBY and MITCHELL.

A man, aged 23 years, developed an eruption forty-eight hours previous to presentation. The first lesions were noted when the patient arose in the morning and new ones continued to appear during the two subsequent days. They were situated chiefly on the forearms, dorsal surfaces of the hands and the face.

Large pale red papules were well distributed over both forearms. A few similar papules were scattered irregularly over the face. On the dorsal surface of the hands and wrists were many circinate patches of vesico-bullous lesions. Several patches of dermatitis were present on the lower extremities, composed of superficial papulovesicles with some erythema intermingling. There was no constitutional involvement, and a good vaccination scar was present. On careful inquiry it was ascertained that the patient had been taking a patent medicine for rheumatism which on analysis was found to contain potassium iodid.

The sudden appearance of the eruption, together with the striking resemblance of many of the large papules to variola, in addition to the prevalence of variola at present made the case interesting.

DISCUSSION

DR. ORMSBY said that the patient was presented because of the resemblance of many of the lesions to variola, and the epidemic of this disease. He believed the case was probably one of dermatitis medicamentosa from potassium iodid.

TUBERCULOSIS VERRUCOSA CUTIS, LUPUS VULGARIS AND
LICHEN SCROFULOSORUM. Presented by DR. STILLIANS.

The patient was a boy, aged 10 years, an American, of a mentally defective family, not syphilitic. The lesion on the foot appeared in infancy, and the leg lesions appeared later. These had received a half erythema dose of roentgen ray about two months ago; they became moist and tender a week after treatment. About two weeks after the treatment, the chest eruption appeared, became profuse over the chest, arms and thighs, and is now in regression. Examination of the chest showed no signs of pulmonary involvement, and a von Pirquet test made five weeks ago was negative.

DISCUSSION

DR. WILE did not agree with the diagnosis. It appeared to him to be an unusual case of hypertrophic and verrucous nevus. He could see no resemblance to verrucosa cutis in this case, and thought it would conform with those of verrucous nevus.

DR. COLE agreed with Dr. Wile's diagnosis. He thought it was a linear nevus with a lichen pilaris on the arms.

DR. STILLIANS said the first thing to be considered was the history of the lesions appearing just after birth, which did not amount to much as the mother was not normal mentally. The lesions on the leg were said to have appeared a considerable time after the lesions on the feet, and were said not to have been present a long time. When they saw the lesions they were not verrucous as they were at present, but flat, with only a moderate amount of crusting. Under roentgen therapy, one-half an erythema dose, there was considerable reaction—the lesions became painful, and within the past month had taken on the verrucous appearance. Dr. Stillians had thought of linear nevus but believed the lesions were not linear enough, and there was no pigmentation. At the time of the roentgen reaction, the acuminate eruption appeared on the arms, legs and thighs, with an adherent scale. He thought the only possible solution of the difficulty was to call it a lichen scrofulosorum.

FAVUS. Presented by DR. WAUGH.

A boy, aged 5 years, presented a disorder of six months' duration. A number of areas were involved on the scalp; some were roughly circular, atrophic and entirely free from hair; others had small areas of hair remaining. Many crusted lesions were present.

DISCUSSION

DR. WAUGH said the case was one of favus, but was unusual in the extensive involvement in the length of time the disorder had been present. It was first noticed four months ago, and at present there was a patch 3 inches in diameter. Darier had described a type of favus which was contagious and

much more rapid in its spread and extent than the ordinary favus infection. It was of about the same extent as the trichophyton infection of the scalp would have been, and Dr. Waugh thought this was unusually rapid for favus.

TUBERCULOSIS VERRUCOSA CUTIS. Presented by DR. OLIVER.

The patient was a colored man, aged 24 years, whose present trouble began two years ago while in service in France. It began about the external nares, and for over a year remained quiescent, involving only the external nares and upper lip. Within the past eight months only had it involved the entire face.

(This case was first presented before the Society at the December, 1920, meeting, and recorded in the Society Proceedings, ARCH. DERMAT. & SYPH., April, 1920.)

DISCUSSION

DR. HAASE believed the case was one of tuberculosis. It resembled two other things — syphilis and blastomycetic dermatitis — but he thought these could be excluded because there were no miliary abscesses around the border of the lesions. It was possible to express some pus, but many of the sections showed no abscess formation there. The pathology in the histologic section was beneath the epidermis altogether; there were no miliary abscesses, but some acanthosis. It did not look like syphilis, nor did it leave the scarring usually found in these cases, so he was inclined to believe, regardless of the fact that it had spread rapidly, that histologically and clinically the condition was tuberculosis.

CAPTAIN HAMILTON agreed with Dr. Haase, but said he had never seen tuberculosis spread so quickly. He had seen many cases, and the condition usually developed slowly. He did not believe this was a case of lupus vulgaris, and while he was not accustomed to seeing dark colored people, he thought it looked like a tuberculosis verrucosa.

DR. OLIVER stated that the patient had received six injections of arsphenamin without any appreciable effect on the lesions. He thought at first that Dr. Freeman had found blastomyces while the patient was at Camp Dodge, but Dr. Freeman said he had searched in vain for them. The entire picture had changed since Dr. Freeman saw the patient, and it had been only eight months since it had involved the entire face. Histologic examination showed the condition to be tuberculosis and not blastomycosis.

DERMATITIS NEUROTICA. Presented by DRS. STILLIANS and OLIVER.

The patient was a man, aged 55 years, whose present eruption began four months ago, while the patient was in the hospital as the result of a railroad accident. He constantly scratched the skin and pulled off the scabs, ascribing the itching to the presence of numerous small parasites. There were many thin pigmented scars on the chest and the legs and about the neck and face. Many of the papules were capped by blood clots.

DISCUSSION

DR. PUSEY thought it was a case of acarophobia, and that the man had a psychosis. The man thought he had something in the skin and dug the lesions for that reason. He believed it was not a case of neurotic excoriations.

LUPUS VULGARIS. Presented by Drs. STILLIANS and OLIVER.

A man, about 25 years of age, entered Cook County Hospital, Dec. 23, 1920. The lesions on the face had existed for the past seven years. The glands of the neck had been enlarged for the past nine months. Keratitis had been present for one month. There was a scar over the nose with elevation of the left nares. On the left cheek there was a thin scar with dark brown papules in it.

DISCUSSION

Dr. STILLIANS said the case was presented because of the suggestion of lupus erythematosus. The entire nose was scarred and raised, as if it had been ulcerated. On the cheek there was a scar with apparent recurrence of the disorder in the scar.

Dr. ZEISLER considered the case interesting. There was a good deal of scarring, and it had some of the features of lupus erythematosus, but he had made the diagnosis of lupus vulgaris.

A CASE FOR DIAGNOSIS. Presented by Dr. F. W. CREGOR (by invitation).

The patient was a man, aged 46 years, who had had the disorder for nine years. The disorder began on the arms and later spread to the face and the chest. The areas chiefly involved now were the face, neck, chest and parts of the extremities. The skin was deeply infiltrated, bluish red, and normal lines were exaggerated. Many small flat circular papules were present in addition to many infiltrated patches. The urine was normal.

DISCUSSION

Dr. CREGOR stated that he first saw the patient in April, 1920. He was a veterinary surgeon, who gave a history of a papular eruption on the arms, which had persisted as severe, itching, papular lesions. When the patient was first seen the case was diagnosed as lichen planus. The papules were never considered exactly typical, although in places he thought he could see waxy shining papules. On account of the itching and violaceous color of the lesions this diagnosis was made. The disorder had not yielded to treatment, although the patient had received énésol and the usual applications made in cases of pruritus. Dr. Cregor felt that it might be a premycotic condition, or possibly one of the leukemias. Biopsy did not bear this out, nor did the blood picture. Possibly there was some sensitization, and he hoped these things would be presented in the discussion.

Dr. HAASE was of the opinion that the case belonged in the sensitization group. The lichenification, he believed, was largely due to scratching for relief of itching, and this was due to sensitization, probably to horse or cow dandruff. He suggested that the man be removed from his occupation for a while to find out whether improvement would not result.

Dr. PUSEY thought it was a secondary lichenification in a case of chronic eczema due to some systemic process, quite likely a sensitization. It was a type of case seen by every one frequently and very difficult to relieve.

Dr. STILLIANS thought it might be one of the cases of eczema of the hands and face seen in old people with poor excretory power, and would be glad to hear of any developments in the way of sensitization.

BLASTOMYCOSIS. Presented by Drs. STILLIANS and OLIVER.

The patient was a man, aged 49 years, a plasterer, who presented a lesion on the wrist that had been present for the past two and a half years—a verrucous tumor, oozing pus, in which the blastomyces had been demonstrated.

A CASE FOR DIAGNOSIS (LESIONS ON THE LEGS, NOSE, CHEEK AND SIDE OF THE FACE). Presented by Dr. CLARK.

The patient was a woman aged 61 years. The first lesion started on the middle toe of the right foot about twenty years ago. It was a chronic sore which pained a great deal and gradually spread, involving other toes. Red spots then appeared on the leg, and about the same time the skin of the foot and lower leg began to thicken. The process gradually extended up the leg with the red spots always preceding the thickening and swelling. From time to time open sores appeared on the leg. The legs had been practically without symptoms for two years. She had been told many years ago that varicose veins and change of life produced these conditions.

The lesion on the right side of the face had been present for fifteen years with little change. The lesions on the nose and the right cheek were of three or four years' duration with no frequent symptoms. The lesions on the tonsils and the mass in the neck were of about three months' duration and had started as a "cold." There was difficulty in swallowing but no pain. The Wassermann reaction was negative.

DISCUSSION

Dr. WILE said this was the case he alluded to in connection with Dr. Ormsby's case of ulcers on the chest of an elderly woman. This patient was about 60 and had lesions which began in the fortieth year; on the face they were typical of lupus vulgaris. The next condition to be noted was the elephantiasic condition of the legs, with the lesions in that location forming the mass about the ankle.

Dr. COLE recalled having seen cases of elephantiasis associated with lupus vulgaris in Switzerland. He thought Dr. Clark's case was one of invasion of the lymphatic channels with the tubercle bacillus. The case was interesting on account of the elephantiasis. The lesions on the lower extremities he believed to be true lupus vulgaris. In connection with the elephantiasis, he had seen many cases in Switzerland in which there were true tuberculous ulcers. The patients would get a streptococcic infection, erysipelas, and would then develop elephantiasis such as this patient.

Dr. PUSEY said there were many red lesions on the legs and asked whether Dr. Clark regarded these as lupus vulgaris. He thought they might be lymphangiectases. He agreed with the pathologic picture—the lymphangitis as the cause of elephantiasis, but thought the retiform lesions on the leg, rather sharply defined and pearly, might be lymphangiectases.

Dr. GRINDON thought the lesions on the face and right cheek were undoubtedly those of lupus vulgaris, which seemed to him to be of the Leloir type. The points on the legs had the color and the translucent appearance of lupus vulgaris; they were large lupus nodules situated about follicles. He believed it was a true case of follicular lupus which was seldom seen. The explanation of the doughy mass about the ankle advanced by Dr. Wile was probably

the correct one. There was also a far advanced carcinoma of the soft palate, which was an interesting concomitant. The occurrence of carcinoma on lupus was not rare. In all probability the patient had a lupus lesion of the palate, although it was entirely masked by the carcinoma now present.

DR. LIEBERTHAL believed the mass on the right ankle was an absolutely pure tuberculous mass, a spongy tuberculous tumor. He agreed with the opinion expressed regarding the other lesions.

DR. CLARK stated that the patient had suffered from pulmonary hemorrhages twenty and eighteen years ago. Histologic section of the mass in the neck showed it to be a rapidly growing carcinoma. A diagnosis had been made of lupus vulgaris and tuberculous elephantiasis.

It was a particularly interesting case of skin tuberculosis, because the tuberculosis first appeared in the skin of a tuberculous patient (judging by the history of pulmonary hemorrhage) after she was 40 years old. Furthermore, there had been great spontaneous improvement in the individual lesions on the leg and at the same time a marked extension of the affected area and the development of a pronounced tuberculous elephantiasis.

BLASTOMYCOSIS. Presented by DR. STILLIANS.

An Irish woman, aged 40 years, a housekeeper, had a lesion on the buttock which had been present for fourteen years, and one on the face which had been present only six months. On the right side of the face there was a patch 2 inches in diameter, showing typical verrucosities and a sharply inclined deep red border. On the buttock, a scar about 9 inches in length was seen which had a crusted ulcer about $1\frac{1}{2}$ by 1 inch at one border. She had received six injections of neo-arsphenamin and four roentgen-ray treatments.

DISCUSSION

DR. McEWEN said the location of the first lesion to appear in this case reminded him of one of the early instances of blastomycosis seen in the city, in Dr. Hyde's service. In that case there were two lesions on the buttock corresponding to a portion of the line of contact with the toilet seat. In the present case he thought a relationship between inoculation and the toilet seat might be possible.

A CASE OF XANTHOMA DIABETICORUM. Presented by DRs. ORMSBY and FINNERUD.

The patient was a man, aged 26 years, a butcher. The duration of the present eruption was four years. It began on the elbows and gradually spread to the neck, trunk and other parts of the extremities. There had been no previous skin disease. There were slight, or no, subjective symptoms. No treatment had been given, and none of the lesions had disappeared. The patient had always been in good health and fleshy, except that in the past few months he had been rather weak and had lost about 20 pounds in weight, bringing his weight down to about 200 pounds. A Wassermann test, made at his request, was negative. The individual lesions attained full development in the course of a few weeks and remained stationary.

The lesions consisted of discrete and confluent, hard, dry, match-head to small coin-sized, glistening, yellow-red papules and nodules, situated chiefly on the extensor surface of the forearms, palm and back of the hand, back

and sides of the trunk, buttocks and front and back of the thighs. Each had a pink or red base and areola, and many were pierced at the apex by a hair or follicle mouth. There were several hundred lesions in all. The mouth was without noteworthy changes; the breath did not smell of acetone.

At the time of the first examination, about two and one-half months ago, sugar and albumin were abundant in the urine, and the specific gravity was 1.030. On a diet of clear broth, carbohydrate-free bran muffins, and thrice-cooked 5 per cent. vegetables (spinach, cabbage, etc.), he became sugar-free in less than forty-eight hours. As his tolerance increased, fat, protein and carbohydrates (butter, eggs, 10 and 20 per cent. vegetables, meat, etc.) were added up to about 2,500 calories, which enabled him to carry on his work without loss of weight. Although he had not been faithful in his treatment during the past few weeks, the lesions, which showed beginning involution after the first week of management, had more than two-thirds disappeared at the time of presentation.

DISCUSSION

DR. GRINDON said the lesions on the elbows and arms were plainly those of xanthoma diabetorum, but the pedunculated lesions were not.

DR. WILE asked whether or not the patient was found to have diabetes.

DR. ORMSBY stated that when the patient was first seen he had large numbers of lesions, the major portion of which had cleared up under appropriate diet. When first seen sugar and albumin were abundant in the urine. He requested Dr. Finnerud to give further details.

DR. FINNERUD said that when first seen the patient had inflammatory lesions and all of the characteristics of xanthoma diabetorum. Many of the lesions had disappeared since the sugar was kept down, and the remaining ones did not resemble those that were present when the patient was first seen in October. About ten days after he became sugar-free a marked improvement was noted. Soon about half of the lesions disappeared, and they continued to disappear until about Christmas time. He had not been seen for several weeks, because he had been eating candy and drinking and doing everything he was not supposed to do.

DR. PUSEY thought the cases of xanthoma diabetorum were rare considering the number of diabetics, and recalled a recent interesting experience with a patient who had this disorder. A man had come to him twelve or fourteen years ago with xanthoma diabetorum, and the lesions all disappeared under treatment for diabetes. He had seen him a few weeks ago, and he was well and hearty and had had no recurrence. He was enormously fat and an ideal patient to keep up the diabetes, but there had been no return of the xanthoma.

DR. CREGOR said that a few years ago he saw a young lady with 6 per cent. sugar and a ring of xanthoma about the neck, which disappeared on diet. The chain about the neck was as sharply defined and definite as beads when she was first seen.

DR. WILE expressed himself as much interested in the subject of xanthoma diabetorum and xanthoma multiplex. A number of years ago he had made a rather exhaustive and exhausting study of xanthoma in association with Dr. Pollitzer, and had received the impression that there was no essential difference between xanthoma diabetorum and xanthoma tuberosum. Xanthoma diabetorum appeared in connection with glycosuria and disappeared after

this was controlled. This, he thought, was merely a coincidence and was found in association with the cases of cholesterol which occurs in diabetes. The reason—at least he gathered this from his studies—that the xanthoma tuberosum persists is because of the connective tissue lesions. Dr. Wile thought that most physiologic chemists who have been interested in the study of the blood in xanthoma concede that in xanthoma tuberosum and xanthoma multiplex there is a chronic hypercholesterolemia. In these cases the lesions have a chance to multiply and become permanent. In the diabetic type the disease is usually recognized early on account of the concomitant symptoms; the patient is treated for diabetes and the lesions do not have a chance to organize and become permanent.

DR. MITCHELL said that in the last number of the *Annales de dermatologie et syphiligraphie* there was a report of a case of xanthoma in a diabetic, but the disappearance of the sugar in the urine had no effect on the tumors. As Dr. Wile said, these tumors had been present for a long time and had probably become organized. The author insisted that the term xanthoma diabeticorum should be abandoned.

DR. GRINDON felt that the name xanthoma diabeticorum might be wrong, and that it might be found in cases without glycosuria. Such cases had been reported by Hutchinson and others. There was no question, however, that this xanthoma diabeticorum was clinically different from xanthoma tuberosum.

NEW YORK DERMATOLOGICAL SOCIETY

Regular Meeting, Jan. 25, 1921

JAMES M. WINFIELD, M.D., *President*

HYDROA VACCINIFORME. Presented by DR. HOWARD FOX.

Madeline B., a girl aged 7, born in the United States, was one of a family of three children. Her mother had died of influenza; her father was living and well. At 3 years of age she had suffered from measles. She had always had "a delicate stomach," vomiting on slight provocation.

The eruption first appeared in April, 1919, on the arms, in the form of "pea-sized red spots," on the surface of which lesions developed which "looked like blisters," though no fluid was noticed in them. The eruption made its appearance gradually, requiring three months to attain its maximum development. It was accompanied by constitutional symptoms and swelling of the hands and feet. During the following winter there was comparative freedom from the eruption, which, however, again appeared as a rather acute attack in the following spring. At this time she spent several months in a hospital. According to Dr. Charles M. Williams, who saw her at that time, there was a distinct vesicular eruption, mostly on the face, forearms and hands. Some of the vesicles became pustules. While in the hospital she had an exacerbation of the eruption, accompanied by constitutional symptoms. For the past six months she had suffered from severe photophobia due to lesions of the cornea, this being her chief complaint at the time of presentation.

Examination showed her to be a well nourished, intelligent child. On the forehead, cheeks and extensor surfaces of the forearms and hands were numerous discrete, pea-sized, whitish, slightly depressed pitted scars. There were

no scratch marks or evidence of former itching, such as thickened skin or pigmentation. There were no vesicles. There was a slight conjunctivitis and marginal keratitis of both eyes causing severe photophobia. This was her chief complaint, the cutaneous lesions causing her little discomfort.

DISCUSSION

DR. CLARK said that he had seen the patient at Dr. Williams' service at the Skin and Cancer Hospital, and at that time it seemed a typical case of hydroa vacciniforme. There seemed to be some question as to whether or not the lesions exhibited on the body might not be seborrheic in character. It might be a case of seborrheic dermatitis on the body, but the child certainly also had hydroa vacciniforme.

DR. WILLIAMS said that the patient had been under his care at the Skin and Cancer Hospital, and at that time exhibited distinct vesicular lesions on the legs, arms and face. They came on in distinct crops and become infected. Congestion was a feature of the case. She also had distinct lesions on the tongue, twice. Exposure to the Kromayer lamp for a few minutes produced distinct vesicles. On account of the vesicular character of the lesions and the scarring, a tentative diagnosis of hydroa vacciniforme was made. Cultures were made, but revealed nothing except the ordinary saprophytes of the skin.

DR. WHITEHOUSE thought there was no question about the diagnosis of hydroa vacciniforme, but there seemed to be some other condition, just what, he could not say.

DR. TRIMBLE agreed with the diagnosis of hydroa vacciniforme.

DR. POTTER also agreed with the diagnosis of hydroa vacciniforme, but thought there was also some constitutional disorder present. There was some difficulty in getting a history from the patient, and the facts given did not quite fit with the symptoms. There was no doubt some constitutional condition present which caused the temperature and the keratitis.

DR. WILLIAMS thought the condition was primarily hydroa vacciniforme, but as Dr. Potter had said, some of the symptoms were peculiar—the sudden rise of temperature and the prostration. The patient had had two or three of these outbreaks, and each time there was an infection of the lesions. The rise of temperature might have been due to the local skin infection, but it seemed out of all proportion to that. She had had the same photophobia last spring as now shown.

DR. HOWARD FOX regretted that he had not had the opportunity of seeing the patient at the outset of one of the attacks. It had been difficult to obtain an accurate history from her relatives.

PEMPHIGUS OF THE MOUTH. Presented by DR. HOWARD FOX.

Mrs. L. K., aged 46, born in Austria, began to suffer from "sores" in the mouth about six months ago. This condition had gradually increased in extent and severity until a considerable area of the mucous membrane of the mouth and tongue was affected. The lesions were very painful, especially when eating, and at the present time she was able to eat only liquid food. About fifteen years ago she had suffered from a "nervous breakdown" and an "irritation of the throat" which lasted two months. Otherwise she had always enjoyed good health. She had been married twenty-six years, and was the mother of eight apparently healthy children. No similar disease had ever affected any member of her family.

On examination there were found numerous superficial ulcerations of the buccal mucous membrane and the tongue which were tender to the touch and bled easily on slight traumatism. On the chest there was a dime-sized reddish macule, where, according to the patient's statement, a blister had previously existed, and which required two months to heal completely. There were also a few bean-sized crusted lesions in the mid-dorsal region which had appeared within a few weeks. The patient was a well nourished, healthy looking woman, of medium height, weighing 170 pounds.

PEMPHIGUS VULGARIS. Presented by DR. BECHET.

The patient, a woman aged 53, from Dr. Trimble's service at the University and Bellevue Clinic, was shown at the Dermatological Section of the Academy of Medicine by the speaker on January 4, with a tentative diagnosis of pemphigus of the mouth. Since that time an extensive outbreak of vesicles and bullae had occurred on the trunk, thus corroborating the diagnosis. The lesions were quite large and generally distributed over the body. The lesions in the mouth had been present for eight months previous to the eruption on the body.

PEMPHIGUS (?) OF THE BUCCAL MUCOSA. Presented by DR. WISE for DR. FORDYCE.

Mr. B. G., aged 66, born in Germany, who had been in the United States for thirty-five years, was a tailor by trade. The eruption in his mouth was of two weeks' duration. The lips and buccal mucosa presented intact pea-sized vesicles and ulcerations, sharply limited to the right side of the mouth. There were also present in the involved area whitish patches like leukoplakia. The Wassermann reaction was negative. There were no lesions on the body.

DISCUSSION

DRS. POTTER, LANE and CLARK agreed with the diagnosis in all three cases.

DR. HIGHMAN said that these cases seemed to confirm what had been his impression for the last two or three years, that even granting that the condition was commonest among the Russian Jews, it seemed to be on the increase in general in New York City. Even up at Mount Sinai where there were very few beds for patients with diseases of the skin, there were eight or ten cases a year on an average. The cases presented seemed typical, the most interesting being those of patients with lesions in the mouth, the site in which the disease usually begins. They seemed to remain localized in the buccal orifice for weeks or months; then the exanthematous stage supervened, followed shortly by death. The most malignant cases are the ordinary fulminating bullous variety; they are much more malignant than the foliaceous or vegetating types.

DR. KINGSBURY said that the case of the woman with lesions on the body was most interesting. When shown at the Academy she had lesions only in the mouth, but now she presented other manifestations of the disease. It was, however, rather dangerous to make a diagnosis simply from lesions in the mouth—even though the subsequent development may bear out that diagnosis. But every vesicular lesion in the mouth is not necessarily pemphigus, and one should be careful not to make a positive diagnosis solely on lesions in the buccal mucosa.

DR. WINFIELD said that he had recently seen two especially interesting cases, one of the patients being a woman in affluent circumstances who had a lesion in her mouth which had appeared and disappeared for over three years; there were typical bullae of the lips and side of the cheek, the tongue also being

involved at times. She had been referred to him by a dentist who considered the condition pemphigus. He was keeping close watch on the case to find whether it developed into pemphigus. In the other case, the patient died in the hospital within three weeks from the time the lesion appeared in the mouth. The lesion of the mouth was shortly followed by an outbreak on the chest, and she became toxic and died in three weeks. She had never had any trouble before, and there was no history of any similar attacks.

DR. HOWARD FOX agreed with Dr. Kingsbury that one should be cautious about making a positive diagnosis of pemphigus when the disease affected only the mouth. The three cases shown presented an interesting series. One of them showed lesions of the mouth alone. In his own case there was a beginning involvement of the skin in addition to that of the mucous membranes, while in the third case there were extensive skin lesions, though at first the eruption was confined to the mouth. There was no doubt about the great discomfort suffered by these patients. His own patient had suffered severe pain in the mouth for six months in spite of treatment by various mouth washes, given by a competent laryngologist. Knowing the value of roentgen rays in many inflammatory skin diseases, he had begun to treat the lesions of the mouth with this agent.

DR. TRIMBLE agreed with Drs. Fox and Kingsbury that it was difficult to make a diagnosis of pemphigus by the lesions of the mouth alone, even though it was known to begin in that location, and frequently remained there for a long time without other manifestations. Patients are apt to have apthous lesions in the mouth, and probably no one could make a diagnosis simply from the mouth lesions. The patient whom Dr. Bechet had shown had had recurring attacks from time to time since last February, though she had never had any lesions on the body until after she had been presented before the last meeting of the Section of the Academy on January 4.

DR. WINFIELD agreed with Dr. Highman's observations about the increasing frequency of this condition within the last few years. He said he had seen several cases recently in other nationalities than Russian Jews.

DR. LANE said that he had recently seen a case of pemphigus in a woman of New England stock, born in Connecticut.

DR. TRIMBLE said that so far as his experience went, about ninety-five out of a hundred cases occurred in Jews.

DR. WINFIELD agreed with this estimate.

DR. WILLIAMS said that he saw his first case about fifteen years ago—one of Dr. Buckley's patients, a Boston woman of pure Anglo-Saxon descent.

DIFFUSE SCLERODERMA — SCLERODACTYLIA. Presented by DR. HOWARD FOX.

A. Z., an Italian woman, aged 38, who had come to America twenty-two years ago, and who had been married for four years and was the mother of one apparently healthy child, had enjoyed good health until about twelve or more years ago when she began to suffer from "dead fingers" and gastric disturbances. The symptoms of Raynaud's disease were first noticed in the index finger of the right hand, eventually all of the fingers and both thumbs becoming involved. These phenomena had gradually become more severe and necroses of the tips of the fingers had been noted during the past two years. The "dead fingers" were especially noted in cold weather or when putting the hands in cold water. The gastric symptoms consisted of loss of appetite and distress after eating, but not vomiting.

On examination the patient showed a typical hidebound condition chiefly affecting the hands, forearms and face. The index fingers were tapering, the thumbs clubbed. There was some ankylosis of the finger and wrist joints, and marked Raynaud phenomena, including necroses of the tips of most of the fingers. There were large, ill-defined areas of light brownish pigmentation on the trunk and flexor surfaces of the arms. The patient was a small, poorly nourished woman, weighing 98 pounds.

DISCUSSION

DR. WILLIAMS said it was a typical case, and then told of a patient with localized scleroderma which improved remarkably in two weeks under pituitary extract treatment.

DR. TRIMBLE said he had had some success with pituitrin in one or two cases of morphea, though he had given three patients with sclerodactylia pituitrin without obtaining any result. In his opinion, this case was practically hopeless. He had observed a similar case for a period of years, and that patient eventually developed tuberculosis of the lungs.

DR. BECHET, in answer to Dr. Fox's question, stated that he had had no experience with pituitary extract in generalized scleroderma, but that in an extensive case of localized scleroderma of several years' duration, in which the entire abdomen was involved, he had administered pituitary extract as a last resort. The disease entirely disappeared after some months.

DR. KINGSBURY said he had not noted the woman's fingers, but skeletally there was no reason to expect good results from pituitrin or any other extract, for the damage was already done and was permanent.

DR. WINFIELD said he had tried pituitary extract in only one case, and saw no good effects. Several years ago he had presented a case of generalized scleroderma before the New York Dermatological Society. The woman died later, and at necropsy she was found to have tuberculosis of the lung and suprarenal glands.

HYPERTROPHIC TUBERCULOSIS OF THE NOSE. Presented by Dr. WISE for Dr. FORDYCE.

Edith C., a colored girl, aged 11, presented herself with an eruption on the nose, of nine months' duration. The lower two thirds of the nose presented a pigeon-egg-sized dark fungus mass, the surface of which was verrucous. The border of the lesion was sharply limited with a few outlying pea-sized nodules. There was a profuse purulent discharge from the nostrils, with a deep rhagade below the right nostril. The submaxillary and submental glands were enlarged.

One brother had died of pulmonary tuberculosis. The patient had a linear scar on the right cornea from a former operation (probably a tuberculous eye condition). The Wassermann test was negative. A biopsy confirmed the diagnosis of a verrucous tuberculosis.

DISCUSSION

DR. TRIMBLE remarked that the rapidity of the process was unusual.

DR. CLARK agreed with the diagnosis, and recommended a single massive roentgen-ray exposure, rather than repeated smaller exposures. He told of two cases, one of them in a patient at the Skin and Cancer Hospital, which had cleared up under an extensive massive dose, and the patient had remained well. This patient should receive a massive erythema dose.

DR. KINGSBURY said he was inclined to think the prognosis was bad in this case, both as regards the spreading of the disease and as to curing the lesion.

SEVERE SCARRING FROM OLD ACNE. Presented by DR. WISE for DR. FORDYCE.

Louis S., aged 30, born in Russia, who had been in this country ten years, a salesman, had had skin trouble for six years. There were extensive pinhead-sized depressed scars all over the face and other parts of the body. On the shoulders, back and hips they reached the size of a split pea. Besides these scars there were many blackheads, pin-point to millet-seed sized, that were easily expressed. The patient admitted picking these lesions freely.

HYPERTROPHIC SCARS FOLLOWING PEELING TREATMENT OF ACNE. Presented by DR. HOWARD FOX.

L. S., a salesman, aged 23, began to suffer from acne of the face and neck two and a half years ago. About eighteen months ago he was treated by a "beauty specialist." As the result of an extensive peeling of the face, he remained in a sanatorium for four weeks. Several months later, at the sites of former pustular lesions, unusually disfiguring keloids of various sizes developed on the cheeks and neck. They had remained unchanged up to the present time. The patient was a vigorous appearing man, inclined to be stout.

DISCUSSION

DR. WILLIAMS called attention to the need of caution in treating acne with the roentgen ray, lest a condition which usually passes in a few years at most should be replaced by permanent atrophy, telangiectases and even epithelioma.

DR. CLARK said the man told a story which might help clear up the patchy appearance. Some plaster had been put on, and when this came off it took off areas of skin where it had been applied. This might explain the patchy, keloidal condition.

DR. HIGHMAN said he did not think one could explain keloids. Some people have them and others do not. This man should receive radium treatment, for there was considerable chance for improving his condition.

As to treating mild conditions with dangerous means, he agreed with Dr. Williams, but the proper use of roentgen rays in acne is not dangerous. Neither did he regard the condition as mild, except in the sense of its not being a serious organic disease. The psychic effect of the condition, especially in women, was such that one should produce as rapid and as early a cure as possible, and there was nothing as effective as roentgen rays for this purpose.

DR. KINGSBURY said that in his opinion roentgen-ray treatment is dangerous for acne, and he did not think it should be used.

DR. TRIMBLE said he did not think roentgen-ray treatment was successful in the keloidal form of acne, especially by the older methods. He had watched cases treated by others, and though eventually the lesions were flattened down, the pigmentation, telangiectasis, etc., remained. He was now treating two keloidal cases with radium, and the lesions had flattened down, though the same unsightly appearance remained, the redness, telangiectasis, etc. Both cases were improved from the standpoint of flattening, but the area and general appearance were about the same as when the treatment was started.

DR. WINFIELD agreed with Dr. Kingsbury that roentgen-ray treatment in acne is dangerous. In the case under discussion it was the only thing to be done, although sometimes these keloids improve of themselves without any treatment.

DR. HOWARD FOX said he intended to try radium in this case. He could not allow the statement regarding the danger of using the roentgen ray in acne to go

unchallenged. He agreed that the roentgen ray was an unsatisfactory and dangerous agent when used in the old-fashioned way without proper measurement. By the modern method of exact measurement by arithmetical computation, as introduced by MacKee, Reimer and Witherbee, it was as safe as giving a measured dose of strychnin. He felt sure of his ground in treating young girls with acne, and in the past five years, during which time he had used the standardized technic, he had never seen an erythema result. He did not consider the method a particularly quick one. The main object in using it was to produce permanently good results. It was only necessary to see patients treated by this method to be convinced that it not only gave the desired results, but was entirely devoid of danger when used with reasonable care.

DR. HIGHMAN corroborated what DR. FOX had said about the results obtained by the modern standardized method of using roentgen rays.

DR. WISE said that while he refrained from referring to his own excellent results, he would call attention to the fact that Dr. MacKee had been treating acne with roentgen rays for ten years, and must have treated several thousand patients in private and clinic practice, and had not had a single bad result. If he had, he would have admitted it. That was pretty good evidence of its value, and its freedom from danger in the hands of experts.

FURUNCULOSIS OF SEVERE TYPE TREATED BY VACCINES. Presented by DR. HOWARD FOX.

The patient was an ex-soldier, referred by the U. S. Public Health Service, at whose request his identity is withheld. He was first seen four months ago, when he presented three large, active furuncles. During the previous fifteen months he had suffered from continual crops of boils, which seriously interfered with sleep and rendered him unfit for work. He had been treated with yeast, salves, surgical methods, and by both autogenous and stock vaccines without any apparent benefit. The Wassermann reaction was negative, and the urine contained no sugar or other abnormal ingredients. Examination revealed a man of medium size, well nourished and of good physique. Scattered over the body, from his ears to his toes, were seventy-five scars (by actual count) of former furuncles. The number of lesions had probably been eighty-five or more, as a number of the scars represented two furuncles occurring successively in close proximity. Under the supposition that the previous failure of vaccine therapy might have resulted from too large doses or too short intervals of time, he was given subcutaneous injections of stock vaccines of *Staphylococcus aureus* at intervals of five days. There was no improvement until after the fifth injection when, although new lesions appeared, they were much smaller in size and less painful. After the ninth injection there were no new lesions of any sort, and for the past two and a half months he had been entirely free from furunculosis. During this time the vaccine therapy had been continued. The dosage at the outset was 400 million, increasing to one billion. Later the dosage was considerably reduced with good effect. No local or other treatment, except vaccine injections, had been given.

DISCUSSION

DR. CLARK said that as a rule he had not had such good results as Dr. Fox had shown. That might be explained by the fact that he had used too large doses, as had been suggested. Frequently when vaccines had failed to cure a furunculosis—by the use of a mixture of iron and sulphuric acid, and by caring for the patient's digestion, both gastric and intestinal, he had been able to

clear up pronounced cases. Dr. Fox was certainly to be congratulated on the results in this case. It was far better than any he had been able to obtain with vaccines.

DR. WHITEHOUSE agreed with all that Dr. Clark had said about the failure of vaccines in furunculosis. It was possible that the failures might be attributed to a lack of some standardized methods and to the rather haphazard way in which the vaccines were prepared and administered. Probably Dr. Fox struck a dose that was correct, and if that feature were borne in mind the results might be better.

DR. HIGHMAN said he could not off-hand recall the number of cases he had treated. At first he had used the autogenous vaccines, with poor results; then he used the polyvalent streptococcus and staphylococcus vaccines, starting with one to two hundred million cocci, repeating the injections every fifth day until he reached one-half billion, and in that way his experience had tallied with Dr. Fox's. The average case can probably be cured by stock vaccines in the manner outlined.

DR. WILLIAMS said that he had obtained some good results with autogenous vaccines. It was probably the best treatment we have for the condition.

DR. LANE said that it was frequently stated that when results were not obtained from the use of vaccines in furunculosis, it was because the physician did not know how to administer them. Dr. Fox had had perfect success in this case. In his experience Dr. Lane said that the results had been varying, and the satisfactory results had been rather in the minority. He never used vaccines to the exclusion of other treatment, and frequently obtained as good results with mild antiseptic baths alone as with baths and vaccines combined.

DR. WINFIELD corroborated what Dr. Fox had said about the vaccine method being the best form of treatment, and that the reason good results are not obtained is because too large a dose is given at the beginning. Referring to the point brought up by Dr. Lane, he said that Dr. Bowen wrote an article on the boric acid bath for generalized furunculosis. Dr. Winfield considered the boric bath a valuable aid in treatment.

DR. HOWARD FOX said that he was as enthusiastic about the use of vaccines in furunculosis as he was discouraged with their use in acne (referring particularly to the acne bacillus vaccine). For a long time he had obtained excellent results with stock vaccines of *Staphylococcus aureus* vaccine in furunculosis. He had been surprised, therefore, at the unfavorable opinions of some colleagues in regard to this method of treatment. He had in mind particularly a long discussion by the Chicago Dermatological Society on this subject. He was, therefore, glad of the opportunity to substantiate his views by treating this exceedingly chronic and severe case of furunculosis. The good result had naturally been gratifying.

DR. WINFIELD took exception to what had been said about mixed vaccines in acne. He had obtained some good results in indurated acne, but the autogenous vaccines are not good because few know how to make them.

ICHTHYOSIS. Presented by DR. WHITEHOUSE.

This patient had come to the Post-Graduate Hospital the preceding day with an eruption about a week and a half in duration, and a rather indefinite history of syphilis, and on examining him these lesions were observed on both sides and on various places on the body. He stated that they would flare up

and get red, and that he had had them since childhood. They were localized areas of ichthyosis-like skin, occurring in various sized patches on the trunk, buttocks and extremities.

DISCUSSION

DR. WISE agreed with the diagnosis of ichthyosis in patches.

DR. WILLIAMS expressed the opinion that the case was ichthyosis of the scattered type. During the war, while examining the men, it was interesting to note the various kinds of nevi and ichthyotic conditions exhibited. All varieties were seen, from a stained appearance of the skin to cases of linear nevi, and all grades between. This was probably one of the many varieties and a curious one.

DR. WHITEHOUSE had nothing to add. It seemed to be a rather uncommon type of ichthyosis in patches. The history of syphilis seventeen years ago might possibly be discounted.

NEW YORK ACADEMY OF MEDICINE, SECTION ON
DERMATOLOGY AND SYPHILIS

Feb. 1, 1921

HOWARD FOX, M.D., *Chairman*

SOME INTERESTING ROENTGENOGRAPHIC OBSERVATIONS IN
THE DIFFERENTIAL DIAGNOSIS OF BONE SYPHILIS. DR.
WILLIAM H. STEWART.

I have not prepared a formal paper, but will attempt to show you a few interesting cases, and some of the points which are particularly valuable in the roentgenographic diagnosis of syphilis of the bones.

I have been surprised to find, while visiting various hospitals, that frequently many lesions which are clearly not syphilitic have been so diagnosed. By showing you a few slides of these typical cases, you no doubt will be better able to differentiate between syphilis and other lesions of the osseous structures. Of all the diseases which involve the bones, syphilis is the one characterized by its atypical forms; therefore, I have practically adopted the plan of showing only the typical cases.

In addition to the roentgen-ray findings, it is necessary to have a proper correlation of the history and laboratory findings; in other words, perfect "team work" is necessary in order to diagnose a case satisfactorily.

Syphilis, as you know, is divided into two groups—the congenital and the acquired forms. Both show two distinct varieties, the periosteal and the endosteal. In addition, we have a lesion which involves the epiphyses, but the epiphysal variety is not common; it produces a peculiar disarrangement of the configuration at the epiphyses; patches of calcification occur at the epiphysal line with irregularity, and there is a sort of seriated appearance noted roentgenographically.

Syphilis of the flat bones is an entirely different study, the most common lesion being of the periosteal type.

What are the characteristic points in the differentiation of syphilis from other conditions? First, we must be familiar with those that appear in syphilis. As I have already stated, syphilitic involvement of the long bones usually begins at the ends of the diaphysis and in the shaft. The opposite is true in tuberculosis, which occurs most frequently in the epiphysis. The common

form of syphilis involves the periosteum, which seems to be peculiarly susceptible. Syphilis is distinctly characterized by production whereas in tuberculosis there is destruction. With this production there is always hypertrophy; whereas in tuberculosis atrophy is present. The swelling noted in syphilis is almost entirely in the bone substance itself; whereas in tuberculosis it involves the soft parts more particularly. Sinuses are common in tuberculosis, but seldom seen in syphilis. There is a great multiplicity of lesions in syphilis, whereas in tuberculosis they are fairly limited.

One thing in syphilitic osteomyelitis is noticeable—that is, the clinical appearance of the case does not justify the amount of change shown roentgenographically. It is much like syphilis of the stomach and malignancy. Roentgen-ray examination in syphilis shows extensive changes in the formation of the stomach; whereas clinically the patient does not correspond to the roentgen-ray findings. Wherever we find such a picture in a bony lesion, it is strongly suggestive of syphilis.

The syphilitic forms of bone diseases are distinctly low grade; there is little sequestration, and hardly ever the formation of involucrum.

DISCUSSION

DR. LEWALD said that Dr. Stewart had shown a most interesting collection of cases and had covered the subject thoroughly. In regard to Paget's disease of the joints, he said that he had personally studied about twenty cases and was convinced that it had nothing in common with syphilis. The etiology of the disease is still unknown. The suggestion had been made that it had some relationship to the pituitary gland, for it had some characteristics that make for the opposite of acromegaly. He had also known Paget's disease to be confused with secondary carcinoma in the bones of the pelvis and spine. One must also be sure not to confuse a one bone manifestation of Paget's disease with osteomyelitis or malignancy, particularly when there is no involvement of the skull.

XANTHOMA TUBEROSUM MULTIPLEX. Presented by DR. OCHS.

J. D., a girl aged 2 years and 9 months, whose father and mother were living and both well, was a bottle fed baby. When 6 months old the child suffered from convulsions due to gastro-intestinal disturbance. Ten months later it had bronchopneumonia. The child had always been small and underdeveloped. About thirteen months ago the mother noticed some whitish, thickened lines across the knuckles of both hands; then on the finger ends appeared numerous yellowish-white tuberous growths which flattened the ends of the fingers. There also developed typical large xanthomatous tumors on the elbows and smaller ones on the palms and the face, which looked like mollusca contagiosa. There were also some lesions on the jaws and ears and a number on the knees and soles. The neck and trunk showed thickened creased whitish-yellow lizard-like skin with tubercles. The child suffered from a severe pruritus of the body. The urine contained no abnormal ingredients.

DISCUSSION

DR. OCHS said the xanthoma had nothing to do with the pruritus. It was an altogether independent condition.

There was a general agreement in the diagnosis.

ERYTHEMA MULTIFORME PERSTANS OR HEMORRHAGIC PEMPHIGUS. Presented by DR. OCHS.

Mrs. K., aged 43, was well built but somewhat anemic. About four years ago, when she was in her seventh month of pregnancy, a rash appeared on her upper and lower extremities. This rash had a tendency to fade within a week or two, but before one crop had entirely disappeared, a new one appeared. This condition had persisted to date. The eruption, at first, consisted of macules, papules, or at times rather large nodules. They, however, soon became hemorrhagic and developed into bullae. Occasionally a bulla appeared on an apparently normal base. Bullae had also been observed on the inner surfaces of the cheeks. With the exception of a mild degree of secondary anemia, the patient's blood was negative. The Wassermann test was negative, as was the urine. With the protein tests the patient showed multiple sensitization to several food proteins, and gave marked reactions with the proteins of *Streptococcus hemolyticus* and *Staphylococcus albus*. There was no change in the appearance or the severity of the eruption after two months of treatment with the vaccines of these organisms. A biopsy made of a bullous lesion showed, besides the usual pathologic condition caused by a bleb, vascular dilatation, edema and a mild perivascular infiltration, also red blood cells and hematogenous pigment in the tissues. No treatment had influenced the lesions.

ANNULAR SYPHILODERM. Presented by DR. LEVIN.

A. R., a negress, married, aged 30, had had an eruption of the face and neck for the past three months. There was no history of syphilis excepting that of one miscarriage and the death of two children in infancy.

On the face and neck there were numerous dime to dollar-sized annular lesions. The borders were elevated, infiltrated and made up of pinhead-sized papules. The centers were depressed and brownish. The lesions were less prominent than when first seen about two weeks previously. The Wassermann reaction of the blood was + + + +.

ANNULAR SYPHILID. Presented by DR. HOWARD FOX.

L. C. A., a mulatto, aged 29, a domestic, born in the United States, presented a profuse eruption of the face. It consisted of about sixty small, mostly unbroken, circinate lesions, varying from the size of a pea to that of a bean. They were chiefly found on the forehead, cheeks and chin and had been present for two weeks. The patient also presented vulvar condylomas, a general adenopathy, and complained of severe nocturnal headaches. The Wassermann reaction was strongly positive.

GRANULOMA PYOGENICUM. Presented by DR. LEVIN.

S. B., a white boy, aged 17, had a swelling of the lip of six weeks duration. On the vermilion of the lower lip there was a hazelnut-sized, pedunculated, globular tumor, which was covered by a thin, shiny epidermis. At first red, it was now a dirty yellow because of the purulent contents.

DERMATITIS MEDICAMENTOSA (PHENOLPHTHALEIN ERUPTION). Presented by DR. SCHEER.

The patient was a boy, aged 8, in whom the eruption had existed for two years. The eruption appeared two weeks after the administration of diphtheria antitoxin.

The patient's older sister, who brought him to the clinic, stated that he had been given "Ex-Lax" by his mother at intervals of two or three weeks for the past two years until three months ago; since which time no drug of any kind had been given. At the time of presentation the boy's sister stated that he had received "Ex-Lax" on only two or three occasions, the last about six months ago.

The eruption was distributed on the trunk and extremities and consisted of about two dozen lesions. These were oval and circular macules varying in size from that of a dime to that of a silver dollar, and of a peculiar slate or bluish gray color which did not disappear on pressure. At the onset the lesions were said to have been red and to have gradually taken on their present hue. The intensity of color of the lesions had varied from time to time, but the discoloration had never disappeared.

DISCUSSION

DR. ABRAMOWITZ said that the history given by the patients or their families could not always be relied on. The question whether other drugs besides phenolphthalein could produce a similar eruption was under investigation. If the eruption appeared or grew worse after a dose of phenolphthalein then the case could be definitely established.

Drs. Goldenberg and Chargin had presented a case at the Academy in which a similar eruption followed the administration of arsphenamin.³

DR. HOWARD FOX thought a probable diagnosis of "Ex-Lax" (phenolphthalein) eruption could be made by a glance at this case. The lesions in this condition all had a striking similarity, beginning as sharply defined erythematous patches, later becoming pigmented and persisting for a long time.

EPITHELIOMA OF THE TONGUE. Presented by DR. PAROUNAGIAN.

J. S., a man, aged 41, of American birth, married, a clerk, had had a chancre at the frenum twenty-five years ago, which was cauterized. He received no further treatment, and no secondary conditions appeared. He had been married twenty years, and had had two children, 15 and 16 years of age. His wife had had no miscarriages.

About a year ago the patient noticed a whiteness of the tongue. Eight months ago a tumor appeared on the left central portion of his tongue on the dorsal aspect. This gradually increased in size, and at the time of presentation was the size of a five-cent piece. The submaxillary glands were enlarged; the enlargement was most marked on the left side. The patient had smoked from twenty to thirty cigarets daily for the past ten years. The Wassermann reaction October, 1920, was said to have been positive. The Wassermann reaction (Bellevue) on Jan. 11, 1921, was ++. Examination revealed marked leukoplakia of the dorsum of the tongue, an epithelioma of the middle of the dorsum of the tongue (left side) and a submaxillary adenitis. On Jan. 15, 1921, the patient received oxycyanid of mercury (intravenous) $\frac{1}{6}$ grain; January 18, sodium iodid (intravenous), 31 grains, in water, 20 c.c.; January 22, oxycyanid of mercury (intravenous), $\frac{1}{6}$ grain, and January 27, oxycyanid of mercury (intravenous), $\frac{1}{6}$ grain. The tumor was slowly increasing in size.

EPITHELIOMA OF THE TONGUE. Presented by DR. PAROUNAGIAN.

A. S., a man aged 54, a Norwegian by birth, a barge captain, had had a chancre in the sulcus in 1888; he denied secondary infections. He was treated in Philadelphia in 1920 with some intravenous medicine known as "85."

3. J. Cutan. Dis. **37**:622, 1919.

In February, 1920, he noticed a sore on the under surface of the right side of his tongue, near the tip. This had gradually increased in size. The Wassermann reaction, on Jan. 24, 1921, was negative. No adenopathy was present in this case. The patient received radium treatment at the Post Graduate Hospital on January 31, through the courtesy of Dr. Willis. The lesion was transfixated with a needle containing 5 mg. of radium in a nickel casing. It was treated by transfixation for one hour in one diameter and for one hour at right angles to the first treatment.

SYPHILITIC ONYCHOSIS SICCA (AND ONYCHOLYSIS)? Presented by DR. SCHEER.

B. M., a man aged 21, a waiter, was born in Sweden. He gave a history of having had a chancre on the penis three years ago in Sweden. The dark-field examination was said to have shown spirochetes. He received about 100 injections of mercury intramuscularly every five or six days. Eighteen months later the Wassermann test was negative. He received no arsphenamin. A year later he noticed changes in the nails. These began about the same time on all the nails of the hands and feet. The nail of the left middle finger fell off four months ago after a slight injury. The nails were all discolored and were of a dirty grayish brown hue, most marked on the nails of the toes. The nails of the right thumb and middle finger and of the left thumb and index finger were loosened at the distal halves. There were slight transverse lines on some of the nails of the hands, and the same condition was more marked on the toes. There was no scaling; the entire process was dry, showing no evidence of inflammation, and the condition was painless.

DISCUSSION

DR. WILLIAMS cited the case of a patient with deformity of the nails which she had had from birth. The condition was exactly like that presented in this case.

KERATODERMA IN A CHILD WITH ENDOCRINE DYSFUNCTION. Presented by DR. LEVIN.

S. Z., aged 9, was born in Galicia and had been in this country for five months. The eruption was of four months' duration. When first seen, two weeks previously, the skin of the face was red and covered with grayish scabs. The neck and trunk showed pinpoint-sized follicular papules. The skin of the rest of the body was dry. Under treatment with thyroid extract the skin of the face had become intensely red and smoother. Pinpoint to pinhead-sized follicular papules, red and scaly, had appeared and spread along the neck and down the trunk.

General signs included: flat face and small chin; pigmented macules and increased pigmentation at points of pressure; pot belly and umbilical hernia; cryptorchidism; deformity of the left lower extremity; wide separation of the teeth; sparseness of the hair of the eyebrows and eyelashes, and low down growth of scalp hair, etc.

PEMPHIGUS? Presented by DR. ABRAMOWITZ.

A man, aged 55, in whom lesions of the mouth were healing favorably under applications of 2 per cent. chromic acid solution and a chlorate of potash mouth wash, had been presented previously when the diagnosis of pemphigus was seriously entertained.

DISCUSSION

DR. BECHET said that the patient he had presented at the last meeting with a tentative diagnosis of pemphigus of the mouth a week and a half later had developed a typical pemphigus of the body.

LICHEN PLANUS HYPERTROPHICUS. Presented by DR. LEVIN.

A. T., aged 63, a man, married, an Austrian, a button-hole maker, appeared at the Beth Israel Hospital clinic three weeks ago, complaining of intense itching of both lower extremities. An eruption of the left leg had been present for two years, and the right leg was affected five months ago.

Both legs showed elongated thickened patches, were violaceous in color and elevated; and the surface was warty and covered with firmly adherent scales. In the vicinity of the large patches there were several conical, pea-sized purplish papules and dime-sized, round, brownish, atrophic spots. Under treatment the lesions became flatter, less elevated, warty and scaly.

SEVERE SCARRING FROM OLD ACNE. Presented by DR. WISE for DR. FORDYCE.

Louis S., aged 30, born in Russia and ten years in this country, a salesman, had skin trouble of six years' duration. There were extensive pinhead-sized depressed scars over the face and other parts of the body. On the shoulders, back and hips they reached the size of a split pea. Besides these scars there were many blackheads, pinpoint to millet-seed-sized, that were easily expressed. The patient admitted picking these lesions freely.

CHLOASMA; BEGINNING ACRODERMATITIS OF FEET? Presented by DR. SCHEER from Dr. Fordyce's service at the Vanderbilt Clinic.

J. S., aged 37, white, born in Russia, a tailor, had lived in this country sixteen years. He presented an eruption around both eyes, palm sized, sharply defined, with a brownish-red discoloration. When the skin was stretched the discoloration faded, but not completely. It revealed a slight integumentary pigmentation. The hands and feet were cyanotic and cold.

DISCUSSION

DR. WISE said the most interesting feature of the case was the peculiar redness of the face combined with the chloasma; whether the condition on the foot was the same as that of the face, was a question. As Dr. Scheer had said, the condition of the foot was suggestive of acrodermatitis atrophicans. It was not pernio, for that usually involved the toes, and there was no toe involvement in this case. What the condition of the face might be besides the chloasma was difficult to decide.

LUPUS ERYTHEMATOSUS OR LEPROSY? Presented by DR. WISE from the Vanderbilt Clinic.

Roderick H., aged 32, a colored sailor, was born in the British West Indies. He presented himself at Professor Fordyce's clinic with an eruption on his face. The eruption began on the left nostril, extended to the upper lip, traversed the right nostril, and extended up over the nose half way to the right eye, then crossed the bridge of the nose and extended downward to the left nostril. It was violaceous, slightly raised and slightly papular. There was a dollar-sized patch on the middle of the forehead, and a violaceous linear

eruption extended down to the bridge of the nose. The ears were slightly pigmented. A smear from the nasal mucosa was negative. The Wassermann reaction was negative. There were two patches on the left side of the back, irregular, oval shaped, egg-sized, and one patch on the shoulder. There were numerous pigmented maculæ, pea-sized, all over the trunk. There was anesthesia of the left foot associated with a marked callus at the base of the great toe. There was a ptosis of the left upper lid.

DISCUSSION

DR. WISE said that when the patient first came to the clinic the case was diagnosed as leprosy, but a careful examination for anesthesia was negative. A biopsy was made from the lesion on the nose, and it was decided that the condition was a characteristic lupus erythematosus. The leukodermatous areas on the arm and the chest made the case seem obscure, and suggested that the patient had two different diseases—a true lupus erythematosus of the nose and also a possible tinea of the body. Whether or not that was correct, he could not say; but the biopsy certainly showed lupus erythematosus.

DR. HOWARD FOX thought the lesions on the trunk resembled tinea, and if it were not for the biopsy he would be inclined to consider the lesions on the face to belong to the same disease. He had recently seen a number of cases of tinea covering the entire face, in adult whites at Ellis Island. There was nothing in the case suggestive of leprosy.

CASE FOR DIAGNOSIS. Presented by DR. PAROUNAGIAN.

F. H., a man aged 58, born in the United States, single, a houseman by occupation, was first seen that afternoon at the Bellevue Clinic. About two weeks ago, from no known cause, his face began to swell. The patient did not have fever, and felt well. He did not vomit. His face was red. It took a week for his face to become reduced to its normal size.

That part of his right arm from halfway between the axilla and extending to the wrist began to swell one week ago. The upper limit was boggy. The skin was stretched and on palpation gave the sensation of pus; the rest of the arm was enlarged, but was not boggy.

His face and part of the forearm was scaly and there was peeling in large areas. There were no other cutaneous manifestations.

There was a large scrotal hernia on the right side. The Wassermann test on Feb. 1, 1921, had not yet been reported.

DISCUSSION

DR. HIGHMAN said that the condition was probably a cold abscess or cellulitis. Whether due to a fungus infection of unknown nature or to a bacterium causing such an abscess, he could not say. The condition could not possibly be the erysipeloid of Rosenbach found in people handling raw flesh or fish. The condition of the face seemed to be the end process of an exudative inflammation. There did not seem to be any connection between the condition on the face and that on the arms.

CASE FOR DIAGNOSIS. Presented by DR. ABRAWOWITZ.

N. L. (from the Department of Health Clinic), aged 53, a Russian, who had been in the United States for eighteen years, a grocer, married and the father of five healthy children, had an itchy eruption which about eight months

previously started at knee flexures. About four weeks ago the arms became involved. For the past ten days the eruption had appeared on the neck and trunk.

There was considerable scaling on the scalp and forehead, with a moderate rosacea on the nose and cheeks. On the entire neck there were oval patches the size of a five-cent piece, with scaly pink centers and slightly raised borders. The eruption on the chest, back and forearms showed slightly larger oval patches, some olive-sized with central wrinkling and scaly pink borders. The bends of the knees and elbows were free, but there were palm-sized and larger eczematized patches on the knee flexures, thighs and flexor aspect of the upper extremities. The microscopic examination of scrapings was negative.

DISCUSSION

DR. HIGHMAN said that with the eruption on the knees and the long history, the first thing he would think of was some unusual mycotic condition, which sometimes assumed the appearance of pityriasis rubra. It was possible that the lichenified process behind the knees might have nothing to do with the other, and the rest might be interpreted as pityriasis rosea. It was not fair, however, to assume a double diagnosis, and with the superficial study made it might be well to consider an unusual form of mycosis.

DR. WISE said it was difficult to make a diagnosis without a biopsy.

DR. POLLITZER agreed with the previous speakers that it was difficult to make a diagnosis without a biopsy, but there was a probability of its being a seborrheic condition. It rested between that and early mycosis.

DR. WILLIAMS said that the appearance of the lesions on the trunk was characteristic of pityriasis rosea, but that was not borne out by further examination, and unless one could make a diagnosis of two conditions it was not pityriasis rosea. The lesions behind the knees were like those of an ordinary eczema. The diagnosis of a premycotic infiltration did not appeal to him. There was not the gradually fading border, the congestion or thickening commonly seen in that disease. It was not common to see so many discrete patches with mycosis fungoides. Someone had suggested tinea as a possible diagnosis. It was possible to have a profuse tinea over most of the body, but hardly within the short course of this case. In his opinion the most probable diagnosis was an inflamed seborrheic dermatitis. That would account for most of the conditions seen.

DR. HIGHMAN said that a usual concept had been brought out by Dr. Williams—there is no type of pure dermatitis that cannot be simulated by early mycosis fungoides. A wide distribution or disposition of the lesions with spaces of clear skin between them should not negate the diagnosis of mycosis fungoides. Premycosis might simulate any one of a large group of skin lesions, and it was futile to rule that condition out in this case without further study.

DR. WILLIAMS remarked that if the premycotic state simulates so closely all other diseases it would be impossible to diagnose it.

DR. CHARGIN said he had occasion to observe the case for a few days and could not agree with the diagnosis of mycosis fungoides. While the patient had lesions that might be so interpreted, further study was required from the standpoint of pathology before one could make this diagnosis definitely. The history of the case is of importance in considering the diagnosis. The patches on the knee developed nine months ago, and later a few similar lesions appeared on the forearms; but the generalized eruption was of recent date

(ten days) and clinically bore all the earmarks of pityriasis rosea. In his opinion it was a case of pityriasis rosea with a seborrheic eczema.

DR. HIGHMAN, responding to Dr. Williams' comment, said that he had not stated that premycosis looked like all other dermatoses, but that it looked like those of several groups. However, if he did convey the impression to Dr. Williams, he felt that he was at least in the company of Darrier.

KAPOSÍ'S SARCOMA. Presented by DR. LEVIN.

M. G., a man, aged 55, an Austrian, complained of an eruption of the hands and feet of six years' duration. An ulcer on the left second toe was painful.

When first seen about eight months ago, the skin showed discrete freckles scattered over the trunk. On the outer aspect of the left thigh there was an irregular, purplish, flat patch. On the dorsum of the left hand in the region of the knuckles there were several elevated, purplish, globular tumors. Similar tumors were present on the dorsum of the feet, and on the plantar aspect of the left second toe a tumor had ulcerated. At present the tumors on the dorsum of the hand were smaller and flatter, and on his left foot there were several purplish, bean-sized growths. The left second toe was swollen, purplish, and showed on the plantar surface an elevated, granulating ulcerated growth.

LICHEN PLANUS LESIONS OF THE ORAL MUCOSA. Presented by DR. LEVIN.

I. S., a man aged 40, had a generalized itchy eruption of two months' duration. He had a generalized cutaneous eruption of typical papules and pigmented areas. The most noteworthy feature was the presence of pinpoint to pinhead sized elevated, grayish papules on the mucous membrane of the cheeks. These were disappearing under treatment.

DOUBLE INITIAL LESIONS. ERYTHRODERMA CONGENITALE ICHTHYOSIFORME? Presented by DR. PAROUNAGIAN.

E. A., was a man aged 22, single, Swedish, a marine fireman. His father was alive and well. His mother died at the age of 41. Neither had ever had any eruption on the skin. He had six brothers (two dead) and one sister; three brothers were alive and well, but had not been seen since childhood. One brother and one sister were well, but had the same skin condition as the patient. The patient had always been well, except for an attack of scarlet fever at the age of 14.

From early childhood the patient had noticed a nonitchy, scaly, ichthyotic condition of the skin during cold weather. The lesions were most marked on the extensor surfaces, and were characterized by a follicular hyperplasia with erythema. The patient said that in summer the skin became normal. The condition recurred every winter.

The principal locations were the forehead, cheeks, bridge of the nose, ears, neck, arms, legs and trunk. The genital regions were free from ichthyotic lesions. The forearms presented occupational traumas. The backs of the hands did not present follicular plugs.

The patient had a double chancre on the inner surface of the prepuce with inguinal adenopathy. The duration was three weeks. The lesions appeared ten days after exposure. The dark-field examination was positive on Feb. 1, 1921.

DISCUSSION

DR. ABRAMOWITZ said that one did not observe the erythematous condition on the face with the involvement of the flexor aspects of elbows and knees in ordinary ichthyosis or xerosis. He was inclined to agree with Dr. Parounagian in his diagnosis of ichthyosiform erythroderma.

DR. PAROUNAGIAN said that it was his impression also that it was an ichthyosis. Two other members of the family had the same affection. The fact that the condition was better in summer and worse in winter suggested the diagnosis of ichthyosiform erythroderma.

HYPERTROPHIC LICHEN PLANUS. Presented by DR. ROSTENBERG.

A. P., a man, aged 45, born in Austria, whose family and personal history were irrelevant, had developed vitiligo when 15 years old. At the age of 20, he stated, an eruption of small red nodules appeared on his hands, forearms and legs, which were itchy and disappeared in about four months under arsenical treatment. He was then free from any skin trouble until August, 1920, when he again noticed the appearance of small red nodules on the palms and soles, which finally spread over his entire body.

Examination revealed a marked vitiligo involving various parts of the skin and also affecting the pubic hair, which was white. On the back and arms there were a great number of various sized, slightly atrophic patches, probably the remnants of past lesions. There were also a number of scratch marks and bleeding points. On the buttocks and both legs there were a great number of round and elongated and irregularly shaped, dark red lesions, infiltrated and thickened, and covered with adherent horny scales. There were also marked varicose veins on both legs. On the mucous membrane of the mouth and on the tongue there were typical lichen planus lesions.

Three Wassermann tests, taken since August, were negative.

DISCUSSION

DR. WISE said that lichen planus was the nearest one could come to the diagnosis on a casual examination, but the lesions on the tongue resembled leukoplakia; they were sharply circumscribed and hypertrophic and did not have the lacework appearance seen in lichen planus. The lesions on the penis were probably lichen planus, although one could not make a positive diagnosis.

DR. CLARK said he could not get away from the fact of the scarring, due probably to lesions that had been scratched. The man had evidently suffered very much from itching, and had grouped lesions on the back with some grouped scarring, and even though he gave a history of no vesicles one would be inclined to think that the lesions on the back were those of dermatitis herpetiformis. In his opinion the lesions in the mouth did not resemble lichen planus, but were leukoplactic in character.

DR. WILLIAMS agreed with the diagnosis of dermatitis herpetiformis. The lesions were distinctly grouped, were markedly pruritic, left scars, and the man had had the condition for a long time. The lesions on the leg suggested lichen planus, however, they were not typical patches, but rather the horny skin produced by scratching on a not very well nourished skin.

DR. ROSTENBERG said the man had not had recurrent attacks, but stated that he had an attack twenty years ago in Vienna. At that time there was a good deal of discussion about the condition, and it was diagnosed as lichen planus. Since that time he had been free from eruptions until last August.

He stated that the condition started as small indurated papules on the hands, and that he never had any vesicular lesions. The lesions which looked like vesicles were due to the scratching. There was no history of recurrent attacks. In Duhring's disease there would have been a history of frequent previous attacks.

BLASTOMYCOSIS OR TUBERCULOSIS. DR. WILLIAMS.

Dr. Williams reported a case of lesions on the back of the hands previously presented as possibly blastomycosis or tuberculosis. The man was given three injections of arsphenamin, with no improvement. He then received one roentgen-ray treatment, with marked improvement.

PHILADELPHIA DERMATOLOGICAL SOCIETY

Regular Meeting, Feb. 14, 1921

EDWARD F. CORSON, *Presiding*

PROGRESSIVE PIGMENTARY DERMATOSIS. Presented by DR. KLAUDER for DR. SCHAMBERG.

A white woman, aged 50, about eighteen months ago presented an eruption which made its appearance as pigmented areas on the legs below the knees, and which was progressive until the time it was first seen by the presenter in May, 1920. At that time, there were areas described as consisting of brownish pigmented puncta, grouped to form patches in certain areas on the lower legs. The patient said it disappeared for two weeks last summer. The eruption was slightly itchy. The general health was good. Since coming under observation, new areas have appeared elsewhere on the body. Fairly large ones, the size of half a palm, were present on the back and arms. The newer ones seemed hemorrhagic in some places—elsewhere, when not grouped, they resembled telangiectases. The transverse furrows produced by shoes laced at the front of the ankle showed the pigmentary changes. Below the knees slightly scaly, reddish brown areas, about the size of the outline of a hen's egg, existed over the lower patella and tubercle of the tibia. Around the borders of the patches were telangiectases. Areas were present over the fronts of the elbows and the posterior aspect of the left shoulder. The color suggested that the part had been painted with iodine. Small superficial varicosities were noted on the lower extremities, but none was of sufficient size to warrant the name of varicose veins. Dr. Schamberg gave the condition the title of progressive pigmentary dermatosis.

DISCUSSION

Dr. KNOWLES remarked that the patient did scrubbing and exposed the fronts of the knees to trauma. The areas in those situations were consequently thickened and accentuated. The disease was somewhat like angioma serpiginosum, but the color was darker and the location different.

Dr. KLAUDER said that Adamson had reported twelve such cases, all in males, in seven of whom the eruption was limited to the legs. The others had outbreaks on the forearms. The eruption had been described as consisting of punctate bright red macules resembling grains of cayenne pepper. He was convinced that other pathologic conditions than varicosities with subsequent congestion were present. A biopsy had been made, but the report had not yet been received.

DR. WEIDMAN remarked that the lower part of the eruption showed follicles with hemorrhagic stippling. The spots did not entirely disappear on pressure. In situations in which there was exposure to trauma there was more diffusion and thickening. The condition resembled Hutchinson's angioma. The edges were not shaded off as though an accentuation of a milder process existed.

DR. KLAUDER added that while under observation the lesions originated as punctate hemorrhagic spots which later coalesced. Majocchi's disease was to be considered. Subsequent developments and a report on the biopsy would be given at the next meeting.

SYPHILIS? Presented by DR. STRAUSS.

A white man, aged 27 years, had a generalized outbreak which was first noted by him, Nov. 11, 1920. At that time there appeared most of the eruption found on his body at presentation, which consisted of dry flat papules of a pinkish color, most marked on the backs of the hands, elbows, neck, face, buttocks and shaft of the penis. Scales were prominent on their surfaces. Five days ago lesions appeared on the palms and soles, somewhat purplish and rounded, suggesting erythema multiforme. None of the eruption was itchy. Adenopathy was present. No medicine had been taken. The eruption on the face was perioral in distribution, consisting of flat scaly papules. Report on the Wassermann reaction had not been received.

DISCUSSION

DR. KNOWLES thought it was a case of syphilis.

DR. DAVIS said that many of the lesions resembled lichen planus, although he did not believe it to be that disease.

ECZEMA. Presented by DR. WALKER.

A white man, aged 35, presented palms which were rough and fissured. They had been thickened, itchy and scaly for the past five years. The Wassermann reaction was negative. There was nothing abnormal on the scalp. He had received arsphenamin treatment without improvement and had not been benefited by local remedies for eczema.

DISCUSSION

DR. DAVIS thought the diagnosis lay between palmar eczema and psoriasis.

DR. CORSON considered it a type of eczema likely to be favorably influenced by the roentgen rays.

TRICHOPHYTOSIS. Presented by DR. BROWN.

A white man, aged 30, showed two silver-dollar-sized patches on the extensor surface of the left forearm near the elbow. They were moist, denuded of epidermis, fairly sharply outlined and somewhat crusted. Around them there was a scattered folliculitis which the presenter felt was caused by chrysarobin. A curious feature of this case was a phlebitis of the basilic vein, formerly like a hard cord, now much softer. This vessel passed near one of the patches. Finding the *Trichophyton* fungus in the lesion was considered sufficient proof of the diagnosis when added to the clinical appearance of the condition.

DISCUSSION

DR. KLAUDER remarked that finding the *Trichophyton* did not definitely prove the diagnosis. That organism had often been demonstrated on the normal

skin and as an accidental inclusion in other conditions. The case did not look to him like typical trichophytosis.

DR. BROWN added that the condition had lasted three months in spite of ordinary measures for the treatment of eczema.

DR. WEIDMAN thought it could easily be the deep type of ringworm infection. He had seen cases of similar appearance in which the fungus had been present.

LINEAR NEVUS. Presented by DR. KATZENSTEIN.

A white girl aged 11, had an elongated patch on the scalp at the temple. It had been noted for a year and a half. It measured 5 by 1.5 cm. Of a salmon color, it had a soft papillary surface, somewhat raised above the surrounding scalp. Under roentgen-ray treatment it had reduced one-third in size.

DISCUSSION

DRS. KNOWLES and WALKER considered it a case of linear nevus.

CASE FOR DIAGNOSIS. Presented by DR. DENGLE.

A white man, aged 67, some years ago, lived for a considerable time in Mexico. The eruption began a year ago, with the appearance of small nodules which grew to the size of a pea in many instances. About fifty in number, they were scattered over various parts of the body, somewhat grouped on the hands, feet, forehead, lips, forearms and thighs. They came out in crops and have persisted without retrogression. No ulceration occurred and anesthesia was doubtfully absent. The nodules were firm, rounded, elevated and slightly itchy. The Wassermann reaction was negative. A biopsy showed granulomatous tissue with a lobulated arrangement and numerous acid-fast bacilli resembling the tubercle bacilli. There were hundreds in a single field.

DISCUSSION

DR. KNOWLES said that only the verrucous form of tuberculosis cutis would give such numbers of bacilli. He inclined to the opinion that the case was one of lepra.

DR. GREENBAUM agreed that such a diagnosis was a most likely one.

LUPUS ERYTHEMATOSUS. Presented by DR. KNOWLES.

A young white man was brought before the society to show involvement of the skin and vermilion of the lip by this disease. A small irregularly shaped area was present on the bridge of the nose and a slightly larger patch on the lower lip. The condition had existed seven months, improving under local applications of trichloroacetic acid.

RADIUM BURN. Presented by DR. GREENBAUM for DR. SCHAMBERG.

A girl, 8 years of age, had received treatment for vascular nevus at the hands of another physician. The original condition was extensive, involving more than half the face. It had been improved by radium, although a considerable portion of the growth remained uninfluenced. Near the inner canthus of the left eye and adjacent portion of the nose was a crusted, oozing, granulated area which had healed and broken down repeatedly for a year. The presenter considered it a radium burn.

PRURIGO NODULARIS. Presented by DR. GREENBAUM.

A middle-aged white woman had suffered from an itchy eruption on the arms and legs for six years. During this time, she had never been free from the disease. The outbreak consisted of discrete nodules and excoriations. The trunk was not involved. The patient said the lesions started as hives which persisted and finally became nodules. The latter were the size of a small pea. The upper extremities showed more of the eruption than did the lower. It was thought to be a case of prurigo nodularis.

DISCUSSION

DR. KLAUDER agreed with the diagnosis.

DR. GREENBAUM said he was not sure whether there was a definite pathology in this disease which admitted of its differentiation under the microscope.

DR. KNOWLES concluded by assenting to the foregoing diagnosis.

CASE FOR DIAGNOSIS. Presented by DR. STRAUSS.

The patient shown was exhibited at the November, 1920, meeting of the Society. She was 42 years of age and had had this condition for five years. During the last three months the disease had been practically stationary. The appearance was one of dermic atrophy intermingled with nodules. It was generalized and itchy. There was some light pigmentation, especially on the neck. There was quite a sheen on some of the papules, suggesting lichen. Other papules resembled wheals. They varied in size occasionally, but never disappeared entirely.

DERMATITIS MEDICAMENTOSA. Presented by DRS. STRAUSS and SIDLICK.

A white man of 30 years, three weeks after completion of a course of fourteen arsphenamin injections, developed keratoses of the palms and nails and an exfoliative dermatitis. He disappeared from observation, and after some time came back with a garlicky odor to the breath and a history of taking Fowler's solution.

CASE FOR DIAGNOSIS. Presented by DR. GREENBAUM.

A white woman, aged 50 years, had had this disease for one year. On the trunk, legs and upper arms were a few, comparatively large, sharply margined and scaly lesions, some with cleared centers, suggesting in appearance the patches of psoriasis nummularis et annulata. In the situations mentioned the eruption was dry, while on the hands the condition was moist and crusted with a yellowish, damp, crumbly accretion—especially abundant about the nails. On the hands the sharp margination was preserved, but other characteristics of the psoriatic type were lacking. The palms were extensively involved. The disease started as small patches and spread peripherally. There was no Wassermann reaction.

DISCUSSION

DR. KNOWLES suggested that a search be made for fungus. He believed, however, that it was a seborrheic type of eczema or an infection implanted on a psoriasis. There was not enough oozing for a dermatitis repens.

DR. WALKER thought the condition was a seborrheic eczema.

Book Review

SYPHILIS. By LOYD THOMPSON, PH.B., M.D., Physician to the Syphilis Clinic, Government Free Bath House. Second edition. Cloth. Price, \$7. Pp. 486, with 88 illustrations. Philadelphia: Lea & Febiger, 1920.

The second edition of Thompson's text on syphilis brings the subject up to date, and is a more comprehensive volume than the first edition, being increased in size by about seventy-two pages. The section on visceral syphilis, given too little attention in the first edition, has been enlarged considerably. The section on laboratory diagnosis is very complete, and the author has added notes on icebox fixation and on a modification of his own technic for the Wassermann reaction.

As in the first edition, the author fails to classify the lesions of syphilis according to the usual stages, and while the division into stages may not be scientific, as the author states, the student will doubtless find it harder to grasp the subject of syphilodermata from this text because of the lack of that division.

Several errors mar the text, as when, in the discussion of the organism of syphilis, *Spirochaeta pallidum* is used both in the title of the section and in the text. A few pages later the word "pallida" is used properly, but on page 41 we find "pallidum" and "pallida" in succeeding paragraphs. On page 133 the author speaks of the difficulty of differentiating the palmar syphiloderm from dermatitis seborrheica, when the palms have no sebaceous glands and do not have seborrheic dermatitis.

Too much space has been devoted to the details of illustrative cases; for example, nearly three pages are devoted in a book of this size to the record of the case of a patient suffering with complete syphilitic alopecia when more essential material must be left out.

The illustrations are for the most part duplicates of those in the first edition, and are varied and adequate.

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STATISTICAL AND HISTOLOGIC STUDIES OF FORDYCE'S DISEASE *

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PHILADELPHIA

LITERARY REVIEW

In 1896, Fordyce¹ reported Fordyce's disease as a peculiar affection of the mucous membrane of the lips and oral cavity; it has now become well known. Fordyce found spots in nearly every case examined, varying in extent from a few bodies confined to the lips to an involvement of both labial and buccal mucous membranes; both conditions were found in persons who were and who were not related. The younger the person affected, the larger and more grouped were the bodies. As the subject grew older the bodies became more numerous, and judging from their smaller size, underwent atrophy. They were not remarked before puberty and occurred regardless of sex. In most cases a seborrheic eczema was associated. The most important microscopic changes consisted in a degeneration of an unknown nature in the epidermal cytoplasm, and Fordyce was inclined to attribute the affection to this—not to sebaceous glands.

Montgomery and Hay,² in 1897, were the next contributors to our knowledge of this condition. They disagreed with Fordyce and believed that age apparently did not play any important part, for while the condition was mostly seen in adults, yet once at least they observed the spots in an infant. The microscopic examinations of sections from two of the cases showed typical sebaceous glands.

Allen,³ in 1897, presented one case, and in discussion Fordyce said that since writing his paper he had seen additional cases, and in one

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1. Fordyce, J. A.: A Peculiar Affection of the Mucous Membrane of the Lips and Oral Cavity, *J. Cutan. Dis.*, 1896, p. 413.

2. Montgomery, D. W., and Hay: Sebaceous Glands in the Mucous Membrane of the Mouth, *Proc. of the Tenth Annual Session of the Assn. American Anatomists*, 1897, p. 76.

3. Allen, C. W.: Case Demonstration, *J. Cutan. Dis.*, 1897, p. 29.

the lower lip was involved. In two or three other cases the condition was associated with seborrheic eczema of the scalp.

Delbanco,⁴ in 1898, presented a male syphilitic patient with oral Fordyce's disease. The microscopic examination revealed principally a simple hypertrophy of mucous glands. Several men discussed his presentation. Engelmann suggested that the teeth played a part. Schmilinsky referred to a case in which the microscopic examination showed a hyperplasia of the mucous glands. Westberg explained the affection by mechanical irritation; he had observed an analogous condition on the penis. Frankel claimed that the process was inflammatory, but Delbanco said that a microscopic preparation did not confirm this belief. Unna alleged that a case of Baelz's disease of the mouth, which he had worked on, corresponded exactly to that presented by Delbanco.

In 1899, Delbanco⁵ reported its occurrence in a second syphilitic, and said that it was to be expected in syphilitic patients. Frankel proposed to call the condition myxadenitis.

Audry,⁶ in 1899, claimed that each nodule corresponded to a sebaceous gland or a sebaceous gland lobule. He found two types of sebaceous glands present: first, subepithelial sebaceous glands whose structure and relation presented nothing anomalous; second, intra-epithelial sebaceous glands (Figs. 1, 2 and 3). All opened on the surface by an excretory duct. An important point was the lack of association of true hairs, although in some of the better developed subepithelial glands the duct became filled with sheaves of small yellow scales which would represent a rudiment of hairs. He claimed that these glands developed at puberty at the same time as the general hair system; that they were present in children and seldom seen in women. He concluded that the disease was due to embryonal rests.

Later in the same year, Delbanco⁷ again reported the affection, this time in well subjects. He also presented a third case, again in a syphilitic, in whom he felt sure that the bodies became more strongly developed during specific treatment. This time the essential histology was that of sebaceous glands which lay, in agreement with Audry, either deeper in the corium or higher in the epiderm. The epiderm was normal and nothing indicative of hairs could be found. He came to the con-

4. Delbanco, E.: Ueber die Entwicklung von Talgdrüsen an der Schleimhaut des Mundes. München. med. Wchnschr., 1898, p. 1510.

5. Delbanco, E.: München. med. Wchnschr., 1899, p. 459.

6. Audry, C.: Ueber eine Veränderung der Lippen und Mundschleimhaut, bestehend in der Entwicklung atrophischer Talgdrüsen. Monatschr. f. prakt. Dermat. **29**:101, 1899.

7. Delbanco, E.: Ueber die Entwicklung von Talgdrüsen in der Schleimhaut des Mundes. Monatschr. f. prakt. Dermat. **29**:353, 1899.

elusion that the affection depended on an abnormal congenital germinal anlage, which ordinarily became visible at a definite period of life, and which through different influences could attain an excessive development. Thus, in the syphilitic he presented he explained the overgrowth of sebaceous glands during specific treatment on the basis that the mucosa, when salivated, is more exposed to traumatic irritation, such as from decayed teeth.

In 1900, Suchannek⁸ reported an oral case. The microscopic examination revealed typical sebaceous glands. He was the first to emphasize a predilection on the part of the disease for the interdental part of the oral mucous membrane.

In 1900, Heuss⁹ reported his case. He thought the histologic sections resembled rhinophyma, but that they differed from it in the absence of plasma cells. The ducts of the sebaceous glands contained masses of fat and also horny cells, often spirally rolled, which resembled rudimentary hairs. The epiderm in places showed hydropic degeneration. He decided to call the disease acne rosacea of the mouth. He concluded that the new growth of sebaceous glands came exclusively from the rete of the mucosa, and did not arise from the previously formed snared off buds in the mucous membrane or from invaginated aberrant buds dating from fetal times.

Radcliffe Crocker,¹⁰ in 1903, provisionally suggested the name of "pseudocolloid of the lips" from the clinical aspect.

In 1904, MacLeod¹¹ reported a well-marked labial case, and in the same year Hutchinson,¹² quite unaware of any prior reports on the subject, reported "miliun of the prolabium," and compared them to the miliun of the lower eyelid.

In 1905, White¹³ examined 540 persons and of this number fifty, or approximately 10 per cent., were positives for the disease. Nearly all lesions were on the upper lip, but some were on the lower and in the mouth. The ratio of males and females affected was 2:3. The youngest patient observed was 12 years old, the oldest 71. The condi-

8. Suchannek, H.: Ueber gehauftes Vorkommen von Talgdrüsen in der Menschlichen Mundschleimhaut, München. med. Wchnschr. **1**:575, 1900.

9. Heuss, E.: Ueber postembryonale Entwicklung von Talgdrüsen in der Schleimhaut der Menschlichen Mundhöhle, Monatschr. f. prakt. Dermat. **31**: 501, 1900.

10. Radcliffe-Crocker, H.: Diseases of the Skin, Philadelphia, P. Blakiston's Son & Co., 1908, p. 758.

11. MacLeod, J. M. H.: A Case of a Peculiar Affection of the Mucous Membrane of the Lips, Brit. J. Dermat. **16**:145, 1904.

12. Hutchinson, J.: Fordyce's Malady (Miliun of the Prolabium), The Polyclinic, Lond. **8**:6, 1904.

13. White, C. J.: Fordyce's Disease, J. Cutan. Dis. **23**:97 (March) 1905.

tion was most frequently encountered in people between the ages of 20 and 40. Seventy per cent. of the patients suffered from diseases which were intimately associated with disorders of the sebaceous glands; 77 per cent. were dyspeptic. Microscopic examination of one patient disclosed a rhinophymatous condition which was in reality outside the lesion proper—in other words, the disease itself was beyond the domain of the glands. White concluded that the essential change lay in the epidermis and consisted of acanthosis, edema and parakeratosis, thus agreeing with Fordyce, the original investigator of the disease.

In 1909, Fordyce,¹⁴ in commenting for a third time on the disease, said it is still a disputed question as to how these bodies originate and whether they are dependent on the presence of sebaceous glands on the mucous surfaces.

In 1913, Pringle¹⁵ reported an extensive case.

Sutton,¹⁶ in 1914, in a histologic examination of three cases, found well developed sebaceous glands. In places they were confined to the subpapillary regions, but in other specimens well defined groups of cells possessing the characteristics of sebaceous glandular substance were found scattered through the rete. In some of the specimens structures somewhat resembling rudimentary hairs were found. Sutton concluded that Fordyce's disease was due to the abnormal presence of sebaceous glandular elements in the epidermis and corium of the mucous membrane lining the mouth and that the yellow coloration of the lesion was due to the collection of fatty matter in the rete. The sebaceous glands probably sprang from invaginated aberrant buds dating back to fetal times.

In 1919, Little¹⁷ believed he had seen instances of Fordyce's disease with quite unusual frequency in lichen planus.

STATISTICAL STUDY

This was based on the examination of 248 persons—127 males and 121 females of all ages. It was conducted by examining groups of persons of about the same age, such as high school and college students, patients in children's hospitals, older ones in the city hospital wards.

14. Fordyce, J. A.: *Some Affections of the Oral and Nasal Cavities which Are Related to Skin Diseases*, New York M. J., 1909, p. 467.

15. Pringle, J. J.: *Fordyce's Disease*, Proc. Roy. Soc. Med. London, Dermat. Section 7:48, 1913-1914.

16. Sutton, R. L.: *The Histopathology of Fordyce's Disease*, J. M. Res. 29:489, 1914.

17. Little, E. G.: *Lichen Planus*, J. Cutan. Dis. 37:649, 1919.

and others. The results are therefore representative of all classes of society. The findings have been distributed under different headings, and a compilation of them gives the following data:

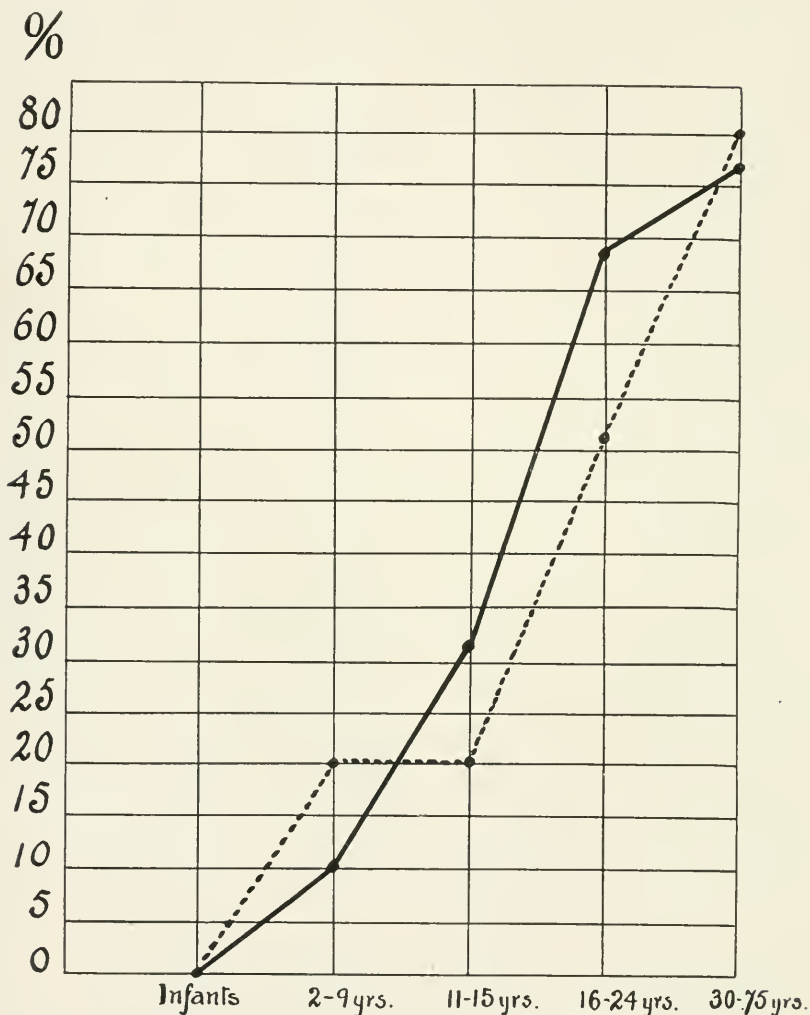


Fig. 1.—Incidence of Fordyce's disease according to age and sex, 248 cases (arranged from Table 2); solid line, males; broken line, females.

The following points stand out in the several tables:

Table 1: Considering the disease regardless of the age of the patient, males and females are about equally affected.

Table 2: The spots were not observed once in infants (below 4 weeks of age in our series). Their incidence increases with age in both

males and females (see chart). They occur earlier in males than in females. After the age of 30 their incidence in males and females is the same. Seventy per cent. of all persons above the age of puberty exhibit these spots.

Table 3: As to well-marked cases (referring to the total number of spots and irrespective of location), these occur earlier and are more frequently found in males.

Table 4: In regard to focal distribution (upper lip, lower lip, mouth), sex and age have a part as follows:

(a) In the earlier age group (16 to 24 years) the spots in females have a severer local restriction than in males, that is, they are restricted to the upper lip. If mouth lesions appear, they will be seen more frequently with advancing years. This applies to both males and females, but especially to females. In the latter mouth spots appear three times more frequently in later periods than in earlier.

(b) Lip and mouth together are affected at all ages more commonly in males than in females.

Isolated clinical data which the tables do not bring out are:

The youngest age at which they were observed was 3 years, the oldest 85 years.

The range in number of spots extended from five to ten up to hundreds.

The lower lip was never the only part involved. If affected at all, it was as part of an extensive case.

We agree with Suchanek that oral spots tend to be limited to the interdental region.

In two cases one or two yellowish, shot-sized tumors were present in the center of a cluster of Fordyce spots in the mouth. These were doubtless small sebaceous cysts. In only three persons was any other pathologic alteration noted, and this was limited to a moderate hyperemia around and between the spots.

HISTOLOGIC STUDIES

These have to do with the basic nature of Fordyce's disease.

Our histologic material consisted of forty-three blocks of tissue excised at necropsy from fourteen human subjects and three monkeys. In all but one or two of these, owing to their being "unclaimed" bodies, we were able to remove both lips in their entirety and all of the buccal mucosa. The incisions included one centimeter or more of skin externally, pierced the whole cheek and passed fully to the gingival margins and behind the last molars within the mouth. This mass was then removed to the laboratory and studied at more leisure (Fig. 2A).



Fig. 2.—A, fresh, untreated postmortem specimen showing scope of material examined; natural size; *s d* is the orifice of Steno's duct. B, selected portion of A after fixation in formaldehyd, and showing experimental tattooing; magnified about ten times. Only the beads of secretion are visible on the surface—not the whole spot as in *a*. C, "map" of position of clinical Fordyce spots as they appeared enlarged about three times under a reading glass, and made before starting laboratory treatment. This is only one of many such "maps." D, same spots as in *c*, and similarly enlarged about three times, after staining with sudan III. Only one, *x*, exhibits traces of the underlying gland in the form of an incomplete pink halo. The others show only the duct orifices and are small, probably unilobular glands.

TABLE 1.—INCIDENCE (248 CASES)

	Patients Examined Total Number of	Positive	Negative	Positive Percentage
Males (all ages).....	127	44	83	35
Females (all ages).....	121	38	83	31

TABLE 2.—INCIDENCE ACCORDING TO AGE AND SEX (248 CASES)

	Infants			2-9 Years			11-14 Years			16-24 Years			30-75 Years		
	No. Posi- tive	No. Nega- tive	Per- cent- age	No. Posi- tive	No. Nega- tive	Per- cent- age	No. Posi- tive	No. Nega- tive	Per- cent- age	No. Posi- tive	No. Nega- tive	Per- cent- age	No. Posi- tive	No. Nega- tive	Per- cent- age
Males.....	0	45	0	1	9	10	7	15	32	17	8	68	19	6	76
Females.....	0	45	0	2	8	20	3	13	20	13	12	48	20	5	80

TABLE 3.—DISTRIBUTION OF WELL-MARKED POSITIVE CASES
(Basis of Sixty-Nine Positive Cases)

	16-24 Years			30-75 Years (50 Cases)			Summary—All Ages (16-75)		
	Posi- tive	Marked	Percentage	Posi- tive	Marked	Percentage	Posi- tive	Marked	Percentage
Males.....	17	8	47	19	6	32	36	14	39
Females.....	13	1	8	20	4	20	33	5	15
							69	19	28

TABLE 4.—DISTRIBUTION ACCORDING TO LOCATION

	16-24 Years					
	Male		Female		Totals	
	No. of Cases	Per- centage	No. of Cases	Per- centage	No. of Cases	Per- centage
1. Upper lip alone.....	6	35	0	60	15	50
2. Upper lip and mouth.....	8	47	2	15.5	10	33
3. Upper lip, lower lip, mouth.....	1	6	0	0	1	3
4. Mouth alone.....	2	12	2	15.5	4	13
Upper lip (1, 2 and 3 above).....	15	88	11	85	26	86
Mouth (2, 3 and 4 above).....	11	65	4	31	15	49

	30-75 Years					
	Male		Female		Totals	
	No. of Cases	Per- centage	No. of Cases	Per- centage	No. of Cases	Per- centage
1. Upper lip alone.....	2	11	2	10	4	10.5
2. Upper lip and mouth.....	12	63	8	40	20	51
3. Upper lip, lower lip, mouth.....	1	5	3	15	4	10.5
4. Mouth alone.....	4	21	7	35	11	28
Upper lip (1, 2 and 3 above).....	15	79	13	65	28	72
Mouth (2, 3 and 4 above).....	17	89	18	90	35	90

	Summary—All Ages (16-75 Years)			
	Male		Female	
	No. of Cases	Per- centage	No. of Cases	Per- centage
1. Upper lip alone.....	8	11	19	28
2. Upper lip and mouth.....	20	10	30	43
3. Upper lip, lower lip, mouth.....	2	3	5	7
4. Mouth alone.....	6	9	15	22
Upper lip (1, 2 and 3 above).....	30	24	54	78
Mouth (2, 3 and 4 above).....	28	22	50	72

Of these fourteen subjects, the spots were visible grossly in nine human patients and in none of the monkeys. The material from the remaining five human patients was used for normal controls. All material was fixed in 4 per cent. formaldehyd.

We used both the frozen and paraffin methods. Ten spots from four different necropsy examinations were immersed in a saturated solution of sudan III for twenty-four hours, differentiated in 50 per cent. alcohol and then the frozen sections were cut. The remaining thirty-three specimens were embedded in paraffin, cut and stained in the routine manner by hematoxylin and eosin. Of the latter specimens, thirteen contained Fordyce spots, making a total of twenty-three spot-containing blocks of tissue sectioned either by the frozen or paraffin technic. Thirteen human and seven monkey blocks were cut as normal controls.

The propositions of the histologic studies were three: (1) to determine whether sebaceous glands are or are not present in relation to the

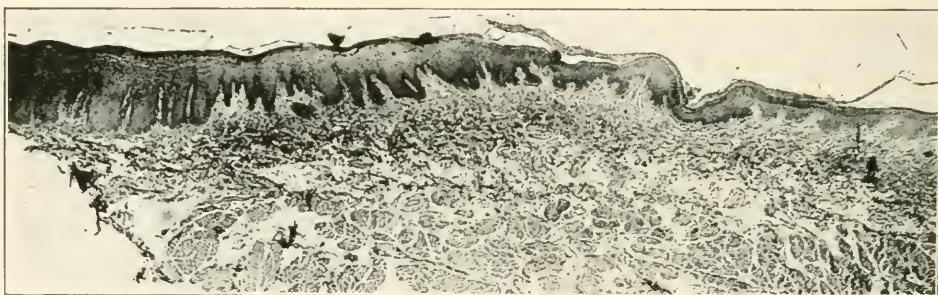


Fig. 3.—Hyperkeratosis and acanthosis adjacent to a Fordyce's spot. Grossly this resembled leukoplakia.

spots; (2) to determine whether the spots seen clinically might be at least referable to such sebaceous glands, and (3) to ascertain whether what we observe clinically as a spot is the gland itself.

Proposition 1.—To Determine the Presence or Absence of Sebaceous Glands.—This was a simple matter, and we promptly found sebaceous glands in sections, as might have been expected when so many workers on the subject had already done so; but our examinations were rewarded by certain additional findings.

We found that after fixation in formaldehyd for twenty-four hours the clinical Fordyce spots in all the tissue blocks became fainter, due both to the fading out of the contrasting pink of the living mucous membrane and to the opacity which coincidentally develops in it. In most of the spots the approximate center was now occupied by a minute gray-white bead (Fig. 2 B), and in blocks which were subsequently

immersed in sudan III solution this bead took on an intense red color—the spot as a whole forming a deep pink halo about it (Fig. 2 D). Its invariable presence within the halo or Fordyce spot is important in relation to, and disagrees with, White's observation that his epidermal degeneration occurred lateral to, or at least outside of, the sebaceous gland. He says "the sebaceous element though abundantly present, lies beyond the diseased tissue proper," and "as the photographs show, the sebaceous glands present lie beyond the boundaries of the lesion proper." The bead is doubtless due to expression of fat from the gland as the tissue has shrunk under the influence of the fixative. Frozen sections from ten of the spots in every case confirmed the presence of sebaceous glands, as have also all the paraffin sections (from thirteen spots), making twenty-three in all, which seems a sufficient number from which to draw positive conclusions.

These findings mean that in every case sebaceous glands occurred in relation to the clinical spots. They also establish the fact that Fordyce spots are fatty, but have not necessarily proved that the clinical appearance is due to the sebaceous glands themselves deeper down. There is still epiderm above and collagen around the glands to dispose of, which theoretically might have become fatty secondarily. It is this which has led to the additional procedures indicated under proposition 2 which are to follow. The foregoing observations, however, show beyond a doubt that the condition is at least *referable* to the underlying sebaceous gland. If it were not so, some of the clinical spots ought to appear apart from the red fatty beads and the pink halo, which they never did.

GENERAL HISTOLOGIC FINDINGS

Before proceeding to the second proposition it will be necessary to state in more detail the histologic findings both in respect to the established observations of other workers and to special ones we have brought out. It is surprising how good the histologic detail was in this soft mucous membrane which was taken from subjects dead as long as three days.

The surface epithelium in our positive cases varied within wide limits, as might be expected of subjects dead for different time periods and from different diseases. In one series of sections the epiderm was markedly thinned out over the sebaceous glands, but in most cases it was practically normal in thickness. In others there was a moderate amount of acanthosis and hyperkeratosis (Fig. 3). In several of the cases, both positive and negative (that is, with reference to the sebaceous glands) there was considerable hydropic degeneration in the middle layers of the epithelium. This was probably due to postmortem autolysis. In one of the control cases parakeratosis, acanthosis and

edema of the epithelium were found histologically, which corresponds to White's view of the essential histopathology of Fordyce's disease. It is possible that White's conclusions were the result of one of these coincident and irrelevant epidermal changes, and that he would have modified them on study of more than one block of tissue.

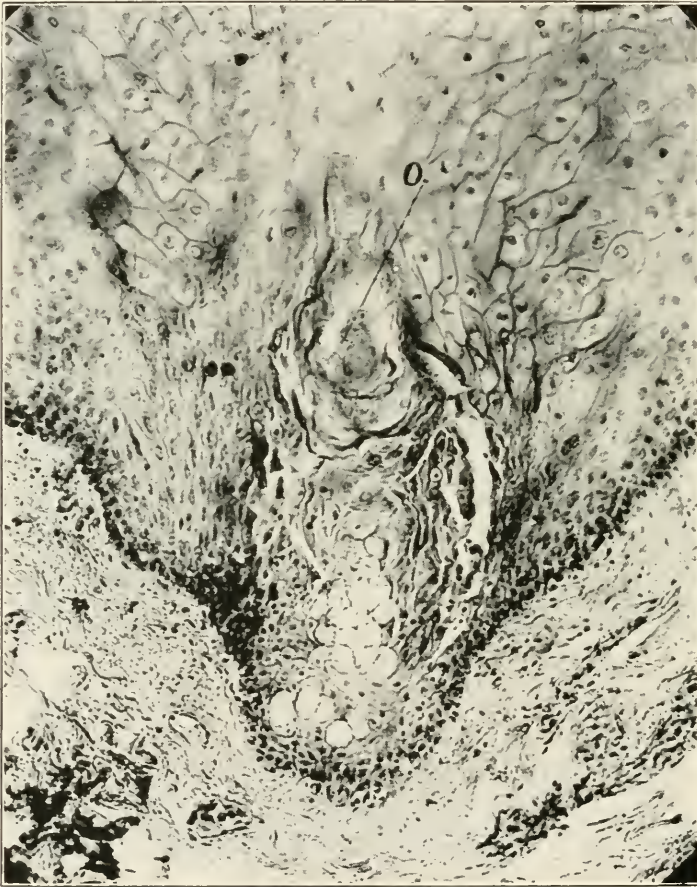


Fig. 4.—Case of Fordyce's disease; sebaceous cells near orifice of sebaceous gland, apparently in rete; *o*, oblique section of duct of the gland.

In regard to the sebaceous glands, as stated before, in every one of the nine necropsy examinations in which the yellowish bodies were seen clinically sebaceous glands were found on histologic examination, and in every position we examined (twenty) in which the yellowish bodies could not be seen grossly, sebaceous glands were not discoverable microscopically. We found various complexities of lobulation in them.

Some were of the form described as "simple vestige" by Sappey,¹⁸ that is, they consisted of a single small pouch. Most of them, however, were typical, fully developed, racemose glands consisting of two or four lobules. They were unconnected with hairs, opening directly on the free surface. We were unable, with Delbanco, to confirm the finding by Audry, Heuss and Sutton of structures that were suggestive of rudimentary hairs.

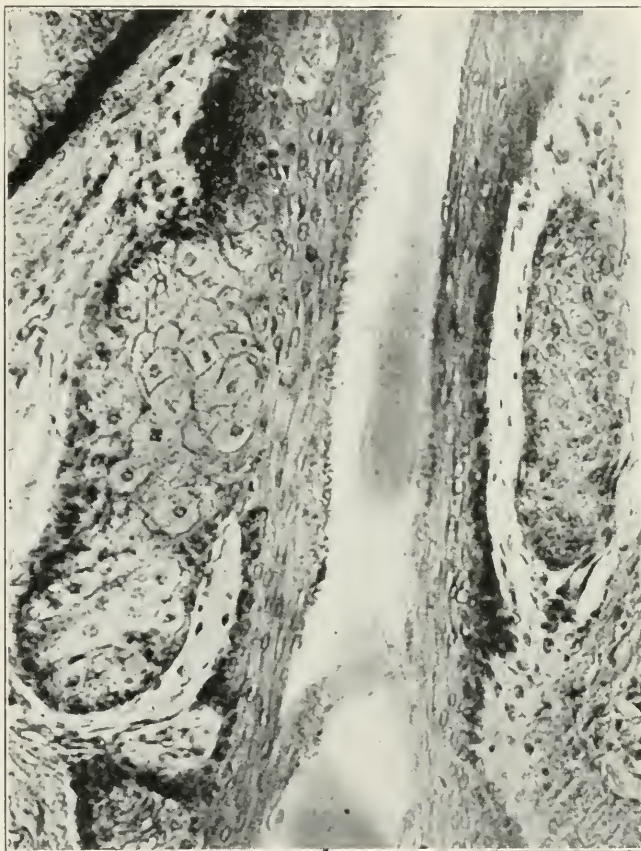


Fig. 5.—Sebaceous cells in continuity with those of hair-shaft, and apparently in a position corresponding to the rete; a condition of the same order but deeper down than that illustrated in Figure 4.

In one of the sections a group of sebaceous gland cells was found apparently within the epithelium at the bottom of one of the interpapillary pegs which penetrated rather more deeply into the corium than

18. Duhring, L. A.: *Cutaneous Medicine*, 1895, Pt. 1, p. 34.

the adjacent ones. However, the spiral arrangement of the more superficial epithelial cells above them (the sebaceous cells) suggested the presence of a duct of a sebaceous gland about which these cells were disposed, and which had evidently been cut tangentially (Figs. 4, 5 and 6). We note this apparently unimportant feature because it may possibly explain the intra-epithelial sebaceous glands seen by Audry, Heuss and Delbanco.

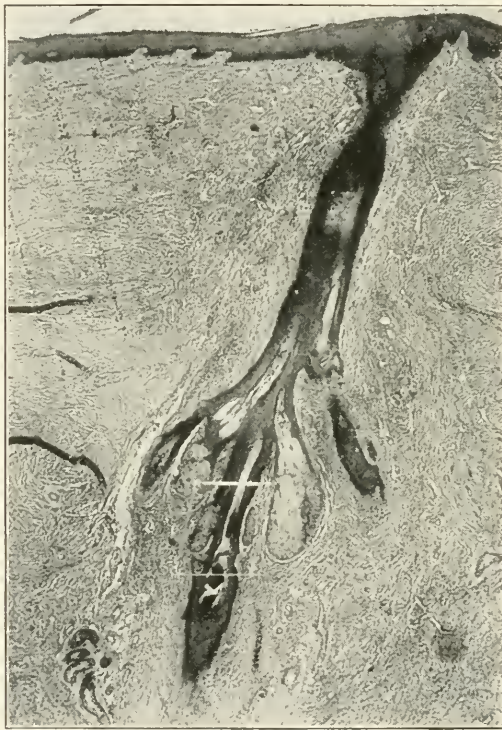


Fig. 6.—Same section as that shown in Figure 5 to show deep position and therefore undoubted sebaceous glandular nature of the elements of Figure 5. The rectangle indicates the part enlarged in Figure 5.

In half of the cases the sebaceous glands were surrounded by a moderate to a marked cellular infiltrate consisting chiefly of small lymphocytes, an occasional plasma cell and mast cells. In a few cases there was a slight diffuse round cell infiltrate within the papillary layer of the corium. Other details of the corium were inconstant, some of the sections showing distention of the capillaries and lymphatic spaces, while in others there was none. One section showed formation of dense hyaloid collagenous bundles suggesting an old scar; all others

had a normal, loosely reticulated corium. The amount of elastica varied considerably in the sections. Sweat glands or hairs were not found in any of the sections.

Proposition 2.—To Identify the Spots Seen Clinically as Referable to the Sebaceous Glands.—This question was treated thus:

A. Mapping Out: The positions of the clinical spots on several of the freshly excised mucosae were precisely plotted on paper with the aid of compasses (Fig. 2C). Both labial and oral specimens were used, involving several square inches of surface in each specimen and including a dozen or more spots. After mapping, the specimens were fixed, washed and immersed in sudan III. The positions of the red (fatty) beads, which indicated orifices of sebaceous glands, and the halos which have already been described were compared with the "map"



Fig. 7.—Experimental incisions marking gross, naked-eye boundaries of a Fordyce spot.

and found to coincide. Expressed mathematically, the clinical spots were found to be equivalent to the red beads and pink halos. The latter were later found histologically to be in relation to sebaceous glands or to be actual parts (ducts) of sebaceous glands. Therefore this procedure of simple gross staining has shown us that the clinical spots are, at least in part, portions of actual sebaceous gland structure (duct orifices) and are always in relation to sebaceous glands.

B. Scarification: A spot was closely surrounded by superficial incisions of the mucous membrane made with a fine scalpel. Histologic examination of the tissue block from the spot showed that sebaceous glands lay between and below the incisions (Fig. 7).

C. Tattooing: A shallow stockade was made around some of the clinical spots with India ink and a fine needle (Fig. 2B). In other

cases the ink was pricked directly into the center of the spot. In every case the black carbon particles were to be found histologically either only around (Fig. 8) or in the center (Fig. 9) of a sebaceous gland. The last two means, scarification and tattooing, have served as tags applied grossly to the clinical spots which have betrayed them microscopically as related to (if, indeed, not) sebaceous glands.

D. Deduction: This point has been considered before. In twenty-three blocks of tissue containing Fordyce's spots clinically a sebaceous

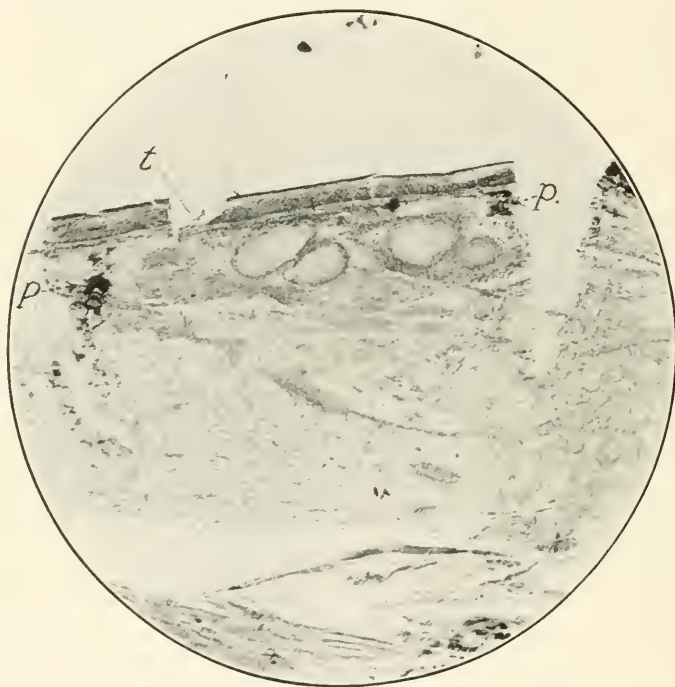


Fig. 8.—Experimental postmortem tattoo marks around a Fordyce spot. Clumps of pigment (India ink) at *p*—more or less in the needle track; *t* is a technical tear.

gland was found every time. In twenty blocks containing no spots, no sebaceous glands were found.

Proposition 3.—To Show That What We Observe Clinically as Spot Is the Gland Itself.—The foregoing results prove that the sebaceous glands are responsible for the clinical spots, and that the spots lie in the same perpendicular trajectory as the gland; that is, we can absolutely eliminate the idea that the sebaceous glands are accidental associates of the clinical spots. The remaining question is, Are they directly responsible, that is, do we see the glands themselves, or is

there some yellow change in overlying tissue which is dependent on the presence of the gland? We have met this proposition by listing the possibilities and eliminating them and by certain direct tests.

Taking up the possibilities first, we feel limited to two "yellowing" processes—fatty and collodial—and to only two structures in which they could occur, namely, the epithelium of the mucosal surface and the collagen of the submucosa. We can eliminate collagen because only once were collagen bundles found that had a broad hyaloid quality. Furthermore, no other observers have even hinted at such a degeneration. With this one exception all the collagen was rather delicately

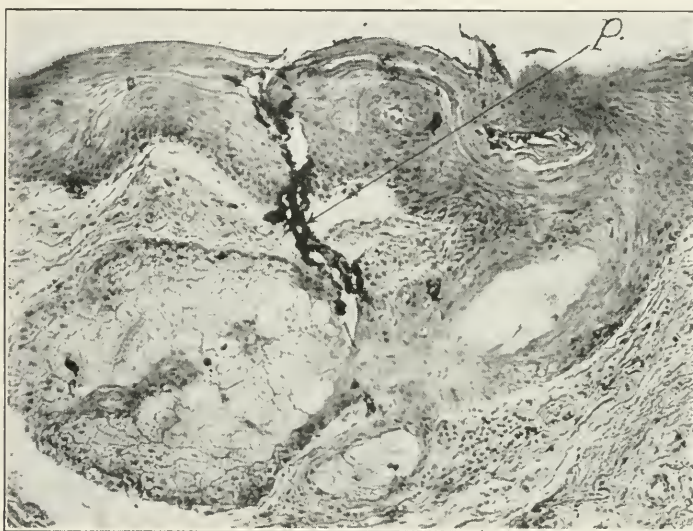


Fig. 9.—Experimental tattoo mark into center of Fordyce spot. Pigment along needle track at *p*.

fibrillar. Fatty changes are more likely than colloid in view of the nearby sebaceous glands. In the first place, they are possible as a fatty metamorphosis of collagen bundles. This we have seen and are familiar with in cases of xanthoma tuberosum and in the tarsal plate of the eyelid around the meibomian glands, but fatty appearances in sudan III properties are so clear cut as not to be easily overlooked, and are lacking in all of our material. Secondly, we have observed areas of normal fat in normal skins (histologically) which have lain unusually high up. We refer to the fatty interstices of the retinaculum cutis, and have considered the possibility that these ectopic sebaceous glands might have determined, or at least been associated with, an unduly high ectopia of such fatty areas also, but actual study shows that they rarely occurred

in our sections and could be dismissed. In the third place, we have carefully studied the surface epithelium for degenerations, because we have disagreed with so high an authority as White.

We report that vacuolization, such as White describes, occurs frequently in our sections, but not as invariably nor as massively as conditions would require. Most important, we have never seen any fat globules anywhere in the epiderm in our sudan III sections—not even in the rete cells directly over these sebaceous glands. We say “even” because rete cells are able to show them. They have been observed by both Pollitzer and ourselves in cases of xanthoma tuberosum and had clearly phagocytosed fatty material from the underlying parts. We agree with White that the degeneration is hydropic, but submit that it did not occur constantly enough in our material to explain the spots, and that the color change to be expected would be

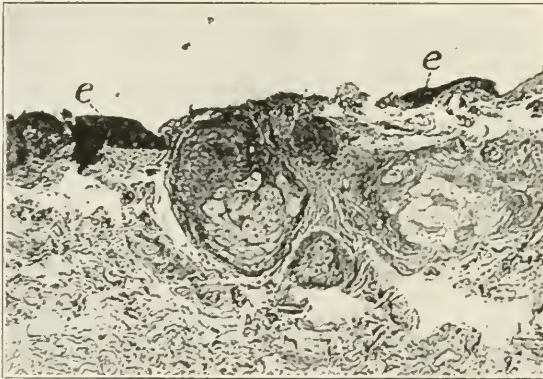


Fig. 10.—Experimentally abraded epiderm over Fordyce spot, showing completeness of removal. The only fragments remaining are shown at *e*, and are insufficient to have been capable of being responsible for the naked-eye yellowing of the Fordyce spot.

a watery or at most a gray one rather than yellow. We have not followed serial sections through every spot in a search for the hydropic degeneration because findings we will consider next make them unnecessary.

These direct tests were made:

A piece of mucous membrane containing the yellow spots was fixed in formaldehyd. The surface was scraped with a sharp blade until we judged that the epithelium was removed. The yellowish spots did not disappear, but undoubtedly became more apparent. On immersion in sudan III the spots stained rapidly. These phenomena are to be explained only on the basis of subepithelial structures.

A strip of fresh mucous membrane containing the spots was treated similarly.

During removal of the surface epithelium the spot continuously slipped out under the knife-blade in a direction opposite to that of the moving blade and in a direction also opposite to that of the surface epithelium. No doubt we were witnessing a movement of an underlying sebaceous gland, which for a time moved away from the point of pressure, but was held to the epithelium after a short excursion by its ductile attachment. After considerable abrasion the spot still remained and on examination with a hand lens exhibited a small perforation in its center from which a small drop of oily material projected. This was evidently the duct orifice and its contained sebum. Histologic examination of this tissue confirmed the absence of the surface epithelium and the presence of sebaceous glands (Fig. 10).

The latter trials appear to us to be in the nature of a finality as demonstrating that a submucous factor is responsible for Fordyce's spots, for we have in both trials witnessed phenomena which were occurring apart from the surface epithelium. In one case the surface was nonexistent, and in the other it was moving contrary to the spot.

PATHOGENESIS

The presence of the glands may best be explained on embryologic grounds. The mouth cavity develops from the stomodeum which forms as an invagination of the ectoblast on the ventral surface of the cephalic end of the embryo.¹⁹ During this process the germinal anlagen for sebaceous glands are carried into the mouth and further develop, about the age of puberty, with the general hair and sebaceous gland system. The common occurrence of the glands in the upper lip and their infrequent appearance in the lower lip is best explained by the natural habit for hair and sebaceous glands to be more numerous on the upper lip, and any dislocation into the position of Fordyce's spots could not be expected to change this numerical habit.

As to the oral cases, the preference of the glands for the region of the interdental line could be explained on the same embryologic basis as facial dermoids occurring in the cheeks.²⁰ The mandibular fissure between the maxillary and mandibular processes unites from behind forward, their incomplete union being represented by the mouth opening (Fig. 11). The line of union from the angle of the mouth backward corresponds roughly to that region of the cheek externally which is opposite the interdental line (Fig. 12). By irregular approximation along this line, portions of the external surface epithelium may be sequestered on the mucosal side and give rise to oral sebaceous glands.

This theory is open to the objection that it does not explain why hair and sweat glands do not also develop in the mouth in Fordyce's disease. This we cannot explain, but that such structures can occur in the mouth is well known, and not alone in the mouth but at other

19. Piersol, G. A.: *Human Anatomy* 1:60, 1916.

20. Bland-Sutton, J.: *Tumors, Innocent and Malignant*, New York, 1911, p. 448.

mucocutaneous regions. Thus, we have studied the lining of a sub-mucous oral cyst referred to us by Dr. T. T. Thomas, in which the sebaceous glands were associated with hairs (but not, so far as we could find, with sweat glands) (Fig. 13) and a hair follicle on the glans penis has actually been commented on and figured as the habitat of the *favus fungus*.²¹ We wish to note in passing that on examination of fifteen vulvas for Fordyce's spots we found one case of hypertrophied labia minora with upward of thirty yellow spots on either inner side, and

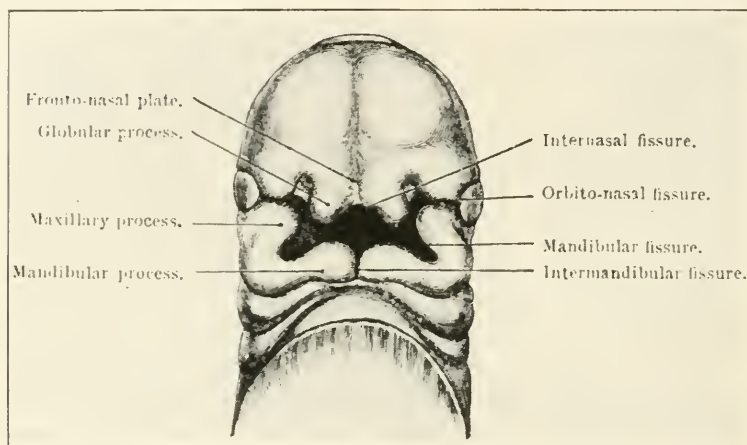


Fig. 11.—Reproduction from Bland-Sutton; head of early embryo. The oral Fordyce's spots are concerned with the mandibular fissure.

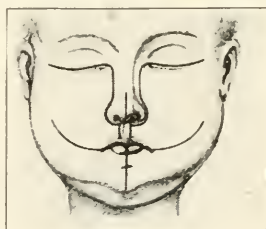


Fig. 12.—Reproduction from Bland-Sutton; the black lines indicate the situation of the embryonic fissures.

that Westberg, in discussing Delbanco's paper, mentioned a condition analogous to Fordyce's disease as occurring on the penis.

CONCLUSIONS

Statistical conclusions are given in brief form in the tables.

From the etiologic standpoint, there has long been a disagreement whether Fordyce's disease is due to degeneration of the surface epithelium (a valid disease) or to the presence of ectopic sebaceous glands,

21. Hardy: *Traité pratique et descriptif des Maladies de la peau*, 1886.

that is, a simple displacement and therefore not necessarily a disease. We feel that the experiments herewith reported have definitely eliminated an epidermal factor for what is seen clinically and on the contrary established the glands as the etiologic basis for the phenomenon.

As to the pathogenesis, the spots are probably due, as Audry and Sutton state, to the snaring off and invagination of germinal anlagen. They increase in size at about the age of puberty *pari passu* with the general hair and sebaceous gland systems.



Fig. 13.—Portion of wall of submucous cyst in floor of mouth with numerous sebaceous glands and hair follicles (Dr. T. T. Thomas' case). Shows possibility of even greater cutaneous inclusions than individual sebaceous glands like Fordyce's spots. Follicle and contained hairs at *h*.

As the condition is present in 70 per cent. of adults, causes no detrimental symptoms and is not a genuine lesion, we agree with Hartzell²²

22. Hartzell, M. B.: *Diseases of the Skin*, Philadelphia, J. B. Lippincott Co., 1919.

that there is doubt as to the propriety of calling the condition a disease; that is, the spots have no pathologic significance beyond that of sebaceous glands elsewhere on the body. But we hasten to add that in spite of the fact that Wertheimer²³ (and probably Kolliker²³ even earlier) observed sebaceous glands in the lip histologically thirteen years before Fordyce's publication, the real credit must still accrue to Fordyce for having brought to clinical light a buried and forgotten scientific observation.

23. Wertheimer, E.: De la structure du bord libre de la levre au divers ages, *Arch. gén. de méd. Par.* **1**:399, 1883.

BLASTOMYCETOID BODIES IN A SARCOMA-LIKE TUMOR OF THE LEG *

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This communication is offered for two reasons: In the first place, it is desired to place on record certain blastomycetoid bodies in order both to obtain information concerning possibly previous reported cases and to supplement cases which may be reported in the future. In the second place, attention is called to the phagocytosis of both normally and abnormally staining elastic fibers both in this case and in proved cases of blastomycosis. For the further study of the latter feature the writer would be grateful for blastomycetic material either in the paraffin block or in the wet.

REPORT OF A CASE

History.—A white woman, aged 23 years, developed a "mole" on the upper portion of the calf four years ago. Stationary for six months, it grew rapidly for the next nine months, attaining the size of a small lemon, when it was removed under local anesthesia. It was not painful, never discharged pus, never ulcerated, was smooth-surfaced, bluish-red and well circumscribed. The patient also had a lump in her right breast the size of a cocoanut, which began several years before the lesion on the leg and exhibited discharging sinuses long before the appearance of the "mole" and was still doing so when it appeared. The enlarged breast antedated her pregnancy.

The operative scar on the leg has healed perfectly, and the breast shows no sinuses. It feels uniformly lobulated, like a hypertrophied mammary gland, with none of the coarse, irregular nodularity to suggest a granulomatous condition. The overlying skin shows a few old small scars.

Laboratory Examination.—The Wassermann reaction was negative. A roentgenogram of the chest was negative for tuberculosis.

HISTOLOGIC EXAMINATION

Material.—This consisted of a spheroidal tumor about 4 cm. in diameter surrounded by a narrow rim of skin. The tumor projected above the surface, and as fixed in formaldehyd was brown and covered with a thin, yellow, loosely attached false membrane. It was not ulcerated. The section surface showed a smooth lined cyst, 2 cm. in diameter, on one side, and on the other a semisolid dirty chocolate-brown material. The latter suggested a sarcoma or extremely bloody granuloma which in large part had undergone liquefaction necrosis to the

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production of a hemorrhagic cyst. As all the material had been fixed in formaldehyd, cultural studies were impossible.

Methods of Examination.—Sections were cut by both the frozen and paraffin technic. In all, several hundred sections have been examined. In part serial, they have been stained by hematoxylin and eosin, thionin, Gram's, Van Gieson's, Mallory's anilin blue for connective tissue, Kossa's silver method and Perl's method for iron. Much of the frozen section work had in view the possibility of dissecting out of bodies from the wet frozen section in case they should have appeared, but this failed in practice because the bodies were so few.

Some of the material has also been digested with antiformin, again having in mind the isolation of the blastomycetoid bodies or mycelia. The latter work has also been impractical because there has been too much detritus (cotton fibers, incompletely dissolved collagen, etc.) to



Fig. 1.—Gross appearance of lesion.

permit a profitable search. Only a few psammoma forms were found. These will be described later.

Results of Histologic Studies.—Nothing abnormal appears in the epiderm except an acanthosis similar to that seen in numerous other dermatoses (Fig. 2). In general it may be said that there were three important features, all limited to the tumor in the corium:

First, a more or less hemorrhagic and disintegrated granulation tissue of extremely vascular character composed most of this tumor. The degeneration and hemorrhage were much more marked toward the center, while in the periphery organization was beyond reproach. The bulk of this tissue was composed of broad capillaries with very distinct and plump endothelial lining cells, and between them there was only a scanty amount of fibrous tissue (Fig. 4). While peripherally it did not widely infiltrate the normal tissue, it was rather definitely limited from it, but without such an individual structure as a capsule. Polymor-

phonuclears were scarce and never concentrated into miliary abscesses as in typical blastomycosis.

The second feature consisted in granulomas which were identical with those of tuberculosis. They were not numerous, and were always placed in the extreme periphery of the tumor. They consisted for the most part of endothelioid cells, showing at most but a few lymphocytes peripherally, and while their centers were sometimes

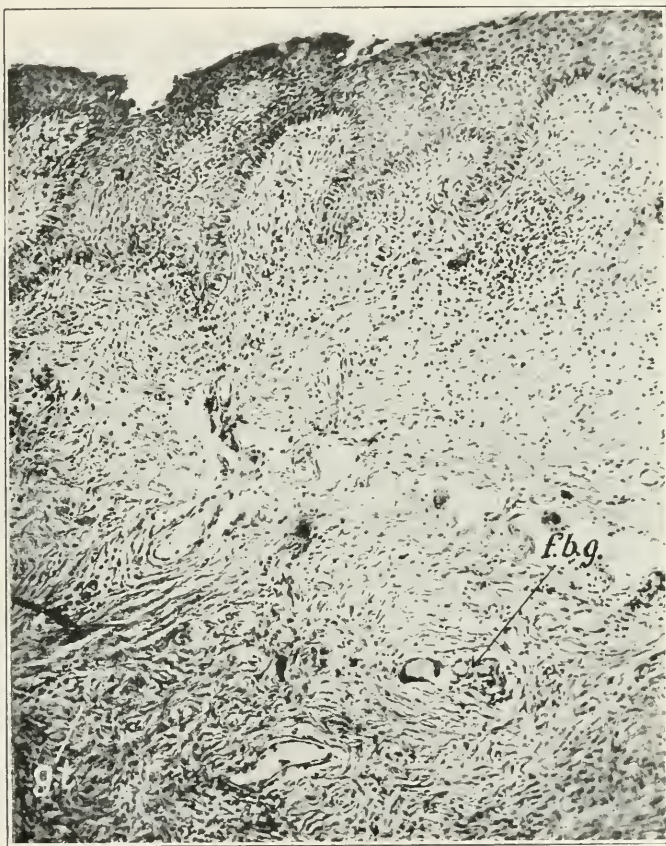


Fig. 2.—General relationships: *g. t.*, granulation tissue moiety of the lesion; *f. b. g.*, foreign body granuloma at periphery of lesion.

necrotic, they were never markedly so. Occasionally a few polymorphonuclears appeared here just as they may in the earliest stages of tubercle formation. Acid-fast organisms have never been demonstrated in them in appropriately stained sections. Small giant cells occasionally appear in the periphery of these granulomas.

The third feature consisted in foreign body granulomas with their giant cells and associated structures.

Giant Cells and Associated Structures.—By the latter we refer to a blastomycetoid body and certain filaments which have turned out to be elastic fibers. The giant cells when fully developed were as large as any seen in tuberculosis, and of typical Langhans type. When seen, they too were practically always in the extreme periphery of the tumor, but never in uniform relation to the tubercles. At times several were



Fig. 3.—Same foreign body granuloma as in Figure 2, more highly magnified; surrounded by vascular granulation tissue.

grouped together and associated with a few lymphocytes to constitute a foreign body type of granuloma. In no case have acid-fast organisms been found. Most often no inclusions were visible. In perhaps only 2 or 3 per cent. of them are the "associated structures" encountered.

The Filamentous Structures.—When these were first noted they were suspected of being mycelial filaments. But in no case were segments discovered; there were no branchings, nor association with

special fruit bodies. Most of the structures stained blue, which was at first regarded as evidence of calcification, but which turned out to be an indication of elacinous degeneration.

The final proof of their elastic nature came in two ways. First, a filament was caught in just the right histologic plane to demonstrate it continuously both in its course within the giant cell, where it was bluish, and outside of it, where it was pink. In the second place, a similar phagocytosis was discovered in hematoxylin and eosin sections of blastomycosis and in those which were especially stained for elastic tissue. The effect of this finding (tempered of course by the lack of large numbers of cases which we like to study before dogmatizing) is to make us suspect that this phagocytosis may be a family trait for

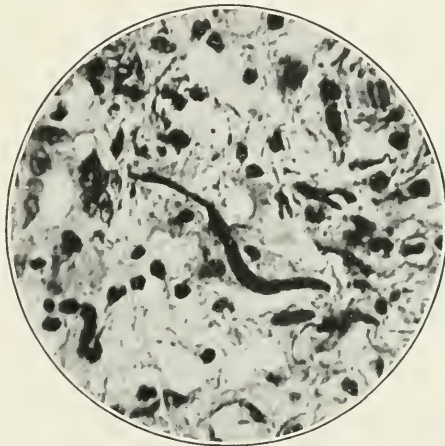


Fig. 4.—Elastic fiber (takes basic dye and is therefore in state of elacinous degeneration) becoming surrounded by giant cell.

blastomycosis; and that, if so, the discovery of such phagocytosis might prove of diagnostic value in obscure cases of blastomycosis. We wish to note in passing that the large numbers of giant cells which are seen in blastomycosis should not be considered as evidence of effort solely against the micro-organism itself. Certainly, in the one case I studied, more elastic filaments were found in giant cells than were blastomycetes. It is probable that other waste tissue products also stimulate the giant cell production; and, finally, with such goodly numbers of the micro-organisms in a free state the question arises whether their enclosure may not really be only an occasional and chance affair by giant cells which have already been evoked by tissue products. There is evidence in this direction in the fact that in foci in which tissue destruction is

complete no elastic fibers will be found in a free state; that is, if present at all, every fiber will be enclosed by giant cells, whereas there are still blastomycetes aplenty which are not phagocytosed.

Blastomycetoid Bodies.—These have been encountered in two forms. As prepared by hematoxylin and eosin, the one stained rusty red, and showed details of structure the better, while the second stained blue. The red form occurred rarely, and we are inclined to look on it as the vital stage because its structural details are better. If this is true, their small numbers must indicate that the infection was on the wane. All

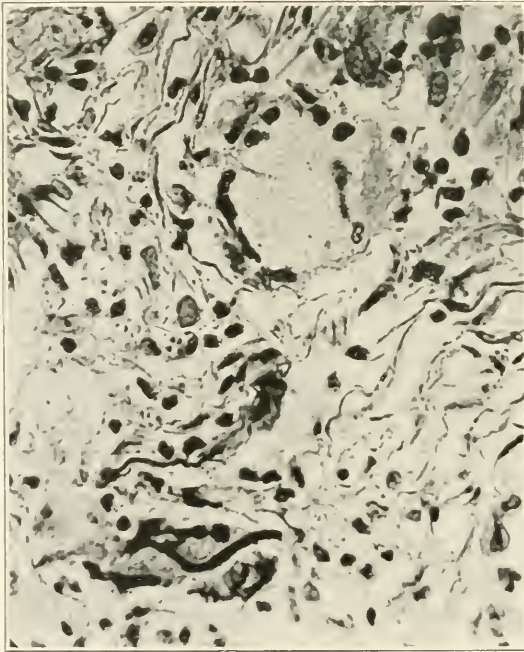


Fig. 5.—Elastic fiber as in Figure 4 but more definitely within giant cell (below); large giant cell above containing no inclusions.

of the red type were found within giant cells. They averaged from 30 to 40 microns in diameter, were spherical or elliptical, and had a thick double contour. Both the shell and the interior were structureless, but the shell had a much denser, glassy quality than the center. In at least two instances a short segmented extension passed from one side like a handle, and in one of these the handle curved sufficiently in the section to be transversely sectioned at the extremity and give the appearance of a tube (Fig. 6). We regard this as a portion of a mycelium.

The Blue Form.—For the most part within giant cells, these were occasionally also to be found free in the granulation tissue. They were of about the same size as the red forms, but differed from them in that they were in several instances clustered (in giant cells) as though budding from a common or approximate point. Again a double contour could often be recognized, but never as sharply as with the red form. Often several lamellae could be made out in them (Fig. 9).

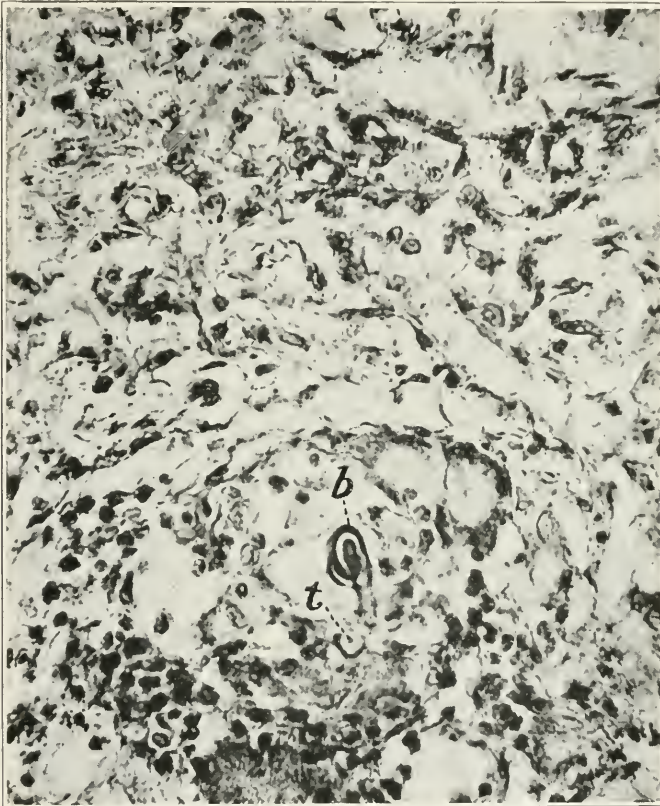


Fig. 6.—Highly magnified body; stained red with hematoxylin and eosin; two giant cells above and to the right of it. The “handled,” downward extension from it is continuous with the transversely sectioned tube at *t* when focusing is done.

The most likely explanation of these is that they are calcified stages of the red forms, and therefore come within the characterization “psammoma bodies.”

DISCUSSION

After a broad survey one concludes that this is a granuloma, and not a sarcoma, for there is far too much fibrous tissue between the capil-

laries to agree with the histology of sarcoma, and the spindle cells are too widely placed even to concede a fibrosarcoma.

We are not at all certain as to what organism is the exciting one. The blastomycetoid bodies seem to be in insufficient numbers to account for such extensive tissue production, unless there be other cyclic forms present which are not brought out by our methods of staining. In a

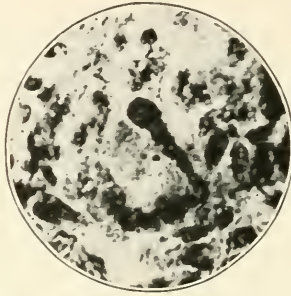


Fig. 7.—Body within giant cell; red with hematoxylin and eosin.

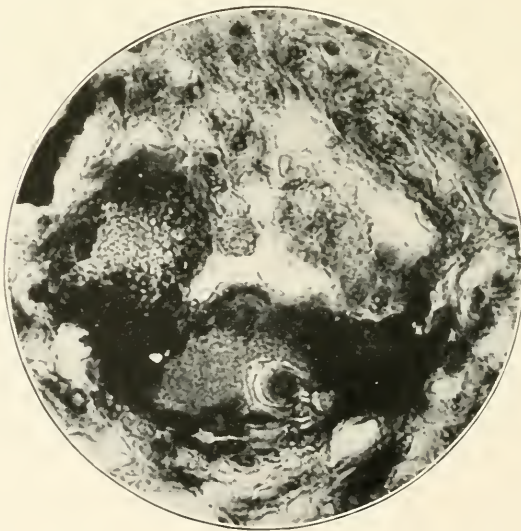


Fig. 8.—Body within giant cell; red with hematoxylin and eosin; double-contoured and showing shadowy "handle" passing toward the right.

similar manner the small tubercles are not sufficiently explainable on the basis of this being a case of tuberculosis because there is such a preponderance of vascular and hemorrhagic granulation tissue. If this be a true blastomycetoid infection it is a different one from Gilchrist's, for both the organism and the tissue reaction are distinctly different.

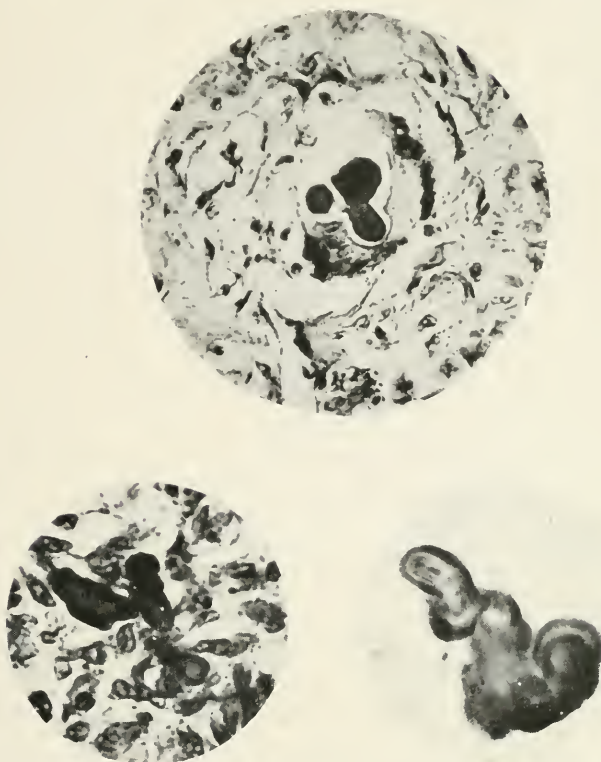


Fig. 9.—Calcified bodies. All stain blue with hematoxylin and eosin; both free and within giant cell. Note similarity of body in Figure 6 to portions of those in this illustration.



Fig. 10.—Body at *b*, calcified, small and probably young; within giant cell, together with its "handle." The handle is continuous above with coarse, deformed cylinder which may be mycelial.

We still have to be content with describing here the circumstances and findings in the case, and entirely omitting, in the absence of possible culture studies, any approach at conclusions concerning its micro-organismal causation. But of one thing we feel certain, and that is that what we have described as blastomycetoid bodies are not tissue products. If not the primary causes of this disease, at least they are secondary invaders. Their size and structure are too constant and definite to be anything else. We have carefully inquired for history of injury or the application of instruments or dressings whereby vegetable tissue could have been forced into the lesion. This has been positively denied.

SUMMARY

A fungous growth on the leg, clinically suspected as sarcoma, was first regarded on histologic examination as lupus vulgaris. Further study showed a vascular granulation tissue, tubercle-like granulomas and blastomycetoid bodies. Elastic fibers were found to have evoked foreign body giant cell production in both this and known cases of blastomycosis.

The cause of the lesion under consideration is left an open question, but it is insisted that the "bodies" are higher fungi and not degenerative tissue products or concretions.

IMPETIGO CONTAGIOSA

RESULTS OF CULTURES MADE OF THIRTY CASES WITH SPECIAL REFERENCE
TO THE CHARACTER OF STREPTOCOCCI ISOLATED *

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BACTERIOLOGIC REVIEW

Impetigo (contagiosa) was definitely described as a clinical entity in 1864 and 1869 by Tilbury Fox.¹ Kohn,² in 1871, concluded that it was due to an organism of the hyphomycete group. In this he was supported by Behrend,³ but this view has been generally abandoned in recent years. Demme,⁴ in 1886, was the first to cultivate a diplococcus from a case of acute contagious pemphigus. Bockhart,⁵ in 1887, concluded that impetigo was caused by *Staphylococcus pyogenes aureus* and *albus*.

In 1893, M. C. Leroux⁶ took cultures from 120 children with cases of contagious impetigo. He obtained seventy positive cultures, finding divers varieties of *Staphylococcus pyogenes* and *streptococci*. He called attention to the contagious character of the disease and its appearance among children in the same family and after contact. Studying impetigo experimentally, he inoculated a series of children, reproduced typical lesions, and on reculture of the lesions found diplococci and the typical streptococci—but no staphylococci. He concluded that impetigo was caused by a special organism to which he gave the name “streptococcus of impetigo.” He concluded that the staphylococci were superimposed organisms which rapidly substituted the streptococci and produced by secondary infection the several clinical manifestations. Davalos,⁷ in 1895, gave as the exciting cause a pseudo-diphtheria bacillus in symbiosis with a virulent coccus. This view has received little encouragement from later investigators.

* From the Laboratory of Dermatological Research, Department of Cutaneous Medicine, University of Pennsylvania and the Department of Dermatology, Jefferson Medical College.

1. Fox, Tilbury: Brit. M. J., 1864, pp. 467, 495, 553, 607; J. Cutan. Med. **3**: 231 (Oct.) 1869.

2. Kohn, M.: Wien. med. Presse, 1871, p. 586.

3. Behrend, H.: Deutsch. med. Wehnschr., No. 48, 1884.

4. Demme, Bern: Verhandl. Cong. f. inn. Med. W., 1886, p. 336.

5. Bockhart, Max: Monatschr. f. prakt. Dermat., No. 11, 1887, p. 450.

6. Leroux, C.: Ann. de dermat. et syph., 1893, No. 4, p. 290.

7. Davalos, J. N.: Zentralbl. f. Bakteriöl. **17**:38, 1895.

Balzer and Griffon⁸ have analyzed fourteen cases of ecthyma and thirty-one cases of impetigo bacteriologically. They found the streptococcus in all. It was present in pure culture in the pus of unopened pustules as a diplococcus or as chains. On culture the organism showed all the classic characteristics of *Streptococcus pyogenes*. Injected into animals it caused erysipelas, abscess and fatal septicemia. Matzenauer⁹ concluded, in 1900, that impetigo contagiosa and pemphigus neonatorum were identical and due to a staphylococcus.

In reference to pemphigus neonatorum it may be proper at this point to review the recent work of Cole and Ruh,¹⁰ and Falls.¹¹

Cole and Ruh, in an epidemic of nine cases of infantile pemphigoid (pemphigus neonatorum), isolated *Staphylococcus aureus* in pure culture in all cases in which the vesicles were unbroken. The epidemic started as a case of typical pemphigoid of the new-born which later changed into a clinical picture of dermatitis exfoliativa neonatorum; and as the etiologic agent was thus the same, they believed there should be no distinction between the two conditions. Impetigo contagiosa, they say, should be sharply differentiated from this infantile pemphigoid (pemphigus neonatorum) because of its different bacteriologic origin. They believed pemphigus neonatorum should be made reportable on account of its high mortality (25 to 50 per cent). They recommended autogenous vaccine.

Falls reported fifty-four cases of pemphigus neonatorum from the standpoint of bacteriology, but did not state from how many cultures were made. He concluded that *Staphylococcus aureus* was the cause.

In 1900, Sabouraud¹² divided impetigo cases into two main divisions—the vesicular type of Tilbury Fox and the pustular type of Bockhart—the first primarily due to a streptococcus which, as a rule, became secondarily associated with staphylococci after which the streptococci died out.

Gilchrist¹³ has reported the results of cultivation in seventeen cases. *Streptococcus pyogenes* was obtained from every case, in ten cases in pure culture. In seven cases *Staphylococcus aureus* was also present, in one case *Staphylococcus citreus* and *albus*, and in another instance a pseudodiphtheria bacillus was present in addition to a streptococcus. Streptococci from only three cases were run through mediums and

8. Balzer and Griffon: Presse méd., Oct. 27, 1897, No. 89, p. 130.

9. Matzenauer, R.: Virchow-Hirsch. Jahrb. d. ges. Med. **25**:549, 1900.

10. Cole, H. N., and Ruh, H. O.: Pemphigoid of the New-Born (Pemphigus Neonatorum), J. A. M. A. **63**:1159 (Oct. 3) 1914.

11. Falls, F. H.: J. Infect. Dis. **20**:86 (Jan.) 1917.

12. Sabouraud, R.: Ann. de dermat. et syph. **31**:325, 1900.

13. Gilchrist, T. C.: Contribution to Science of Medicine by Pupils of W. H. Welch, 1900, p. 409.

identified definitely as *Streptococcus pyogenes*. In one instance he obtained a typical lesion by inoculating the chin with a pure culture of streptococci obtained from the same patient. This outbreak developed five days after the inoculation. These results agree in general with those obtained by Leroux, Balzer and Griffon, and Sabouraud. He concluded that his investigations seemed to indicate that impetigo contagiosa was caused by *Streptococcus pyogenes*.

Bender¹⁴ concluded from cultural studies of twelve cases in 1907 that the cause of impetigo contagiosa was not the white staphylococcus but rather a streptococcus which appeared in chains and gave the typical medium reactions of a streptococcus.

According to Ernst Flehme:¹⁵

In fifty-five cases of impetigo contagiosa investigated bacteriologically, streptococci in pure culture or mixed with staphylococci, according to the age of the lesion, were found. In every case, the organism was of the *Streptococcus longus* type. The organisms always showed hemolysis and acid formation on mannite-litmus-agar. The impetigo streptococci were pathogenic for white mice when large doses of the sediment of bouillon cultures were injected. At the site of injection, a circumscribed purulent lesion was formed. In man it was possible through superficial inoculation to form typical lesions of impetigo, from which the organism was recovered in pure culture. In 15 per cent. of the skins of normal persons, and in 89 per cent. of persons with impetigo, it was possible to demonstrate streptococci which could only be differentiated from the impetigo streptococci by a stronger red tint of mannite-litmus-agar, and hemolysis. The superficial inoculation of pure cultures of streptococci recovered from normal skin likewise produced an impetigo. In addition, scarification of healthy skin on which streptococci were demonstrable, led to the formation of impetigo.¹⁶

His conclusions were that:

. . . the cause of impetigo is the attack on fertile ground of a large dose of impetigo streptococci. The normal skin appears to have a resistance to the organism. The skin of a patient with impetigo has a lessened resistance to the same organism, yet there remains some resistance. One may consider the impetigo streptococcus as a semiparasitic organism, that under certain circumstances and in certain localities, and with a diminished resistance of the skin, leads to the formation of the disease. In addition, during epidemics there may be an increased virulence of the organism which overcomes the normal resistance of the healthy skin.

AUTHORS' WORK

It will be seen from the foregoing that investigators of impetigo have gone no farther than to conclude that a streptococcus was causative or that a streptococcus was the organism most frequently and con-

14. Bender, E.: Arch. f. Dermat. u. Syph. **84**:59, 1907.

15. Flehme, E.: Dermat. Ztschr. **31**:111, 1920; abstr. Arch. Dermat. & Syph. **2**:761, 1920.

16. Quoted from abstr., Arch. Dermat. & Syph. **2**:761 (Dec.) 1920.

sistently isolated from cases of impetigo. It is well known that the streptococcus group is a large one and varies greatly in pathogenicity and biologic characteristics, embracing such widely differing organisms as the almost entirely parasitic pneumococcus on the one hand and the semisaprophytic *Streptococcus fecalis* on the other. We have attempted to go further, that is, we have "analyzed" the different streptococci of impetigo, and have classified them as completely as possible in order to determine, if possible, whether the organisms thus obtained belonged to a single specific strain or whether different members of the streptococcus group were concerned. It occurred to us that the somewhat varying clinical pictures of impetigo might be connected with different strains of streptococcus—just as the markedly impetiginous one of the muddy Flanders battlefields was characterized by heavy *Streptococcus fecalis* incidence.

TECHNIC

We have made cultures from thirty cases of impetigo, all showing lesions clinically typical of this disease. When possible the cultures were made from the serum of unbroken lesions. If not possible, the lesion was scraped with sterile swabs until bloody serum was obtained. In those lesions which had broken and become crusted it was found that cultures were more often positive for streptococci when the swab was taken as deeply as possible. This was similar to the experience of the French bacteriologists with their cultures from wounds; they found that a superficial swab from a wound often resulted in a culture of staphylococci only and the missing of streptococci when they were present.

Swabs were cultivated immediately on 5 per cent. human blood-agar plates, the agar being 0.5 per cent. acid to phenolphthalein and made from fresh beef. After twenty-four hours' inoculation organisms present were picked and seeded for pure culture. Streptococci were repeated on blood agar and picked a second time to insure purity before running them through the carbohydrate mediums for classification. All sugar mediums were made up in bouillon (titrated 0.5 per cent.), to which was added blood serum and Andrade indicator according to the method outlined by Holman.¹⁷

We consider the use of liquid mediums especially important in the identification of the streptococcus group, and agree with the many observers who have stressed the point that solid carbohydrate medium with litmus as an indicator is entirely unsatisfactory for precise work. We attempted the use of solid medium with litmus on several strains and discarded the results, the main difficulty being that it was often

17. Holman, W. L.: Jour. Infect. Dis. **15**:209, 1914; *ibid.* **34**:377, 1916.

impossible to get a satisfactory growth, and it was often doubtful whether there was growth. Delicate color changes were difficult to interpret on solid litmus mediums with stab inoculations.

Along a different line we attempted to produce immune serum in rabbits for agglutination tests. We succeeded in obtaining antiserum which would agglutinate the strain used for inoculation (homologous antigen) in dilutions of 1:100, which was not satisfactorily high. Several strains of streptococci isolated were in a constant state of auto-agglutination, which was impossible to break up even by shaking with sand, and the results on these strains were of course unreadable. The general results of agglutination tests with immune serum agreed with the carbohydrate differentiation tests, that is, the several strains of streptococci which had similar carbohydrate reaction to the strain used for production of the serum were cross-agglutinated, while those with different carbohydrate reactions were not agglutinated. However, the auto-agglutination of several strains and the low agglutination titer (1:100) of serum produced make us hesitate to draw any definite conclusions as to specificity on the basis of our serologic reactions.

We have made no attempt to fulfil all of Koch's postulates, our animal experimentation work having been confined to the production of agglutinins in rabbits.

BACTERIOLOGIC FINDINGS

The bacteriologic findings in the thirty cases examined were: *Streptococci* were found in 24 cases (pure cultures in 10 cases); *Streptococcus pyogenes* 10, *Streptococcus anginosus* 11, *Streptococcus subacidus* 2, *Streptococcus fecalis* 1. *Staphylococci* were found 22 times in 16 cases (mostly associated with other organisms); *Staphylococcus albus* 16 times (2 pure), *Staphylococcus aureus* 6 times (never pure). *Pseudodiphtheria bacillus* was found 4 times, never pure. *Bacillus pyocyaneus* was found once and *Staphylococcus citreus* once.

As to the matter of simple streptococcic incidence, the foregoing data confirm the results of many other investigators who found that a streptococcus was almost invariably present in the lesions of impetigo. This and the successful inoculation tests of several workers convince us that the streptococcus is the causative organism. The staphylococci, pseudodiphtheria bacilli, etc., are secondary invaders.

From the standpoint of the different strains of streptococci, the data show that there are at least four concerned, and the probability is that on examination of a larger series of cases additional ones would appear. *Streptococcus anginosus* and *Streptococcus pyogenes* appear to be most numerous (and equally) important. We have followed the classification of Holman in our work. It will be noted that all the

streptococci which we found were hemolytic save one (*Streptococcus fecalis*), and this was encountered only once.

We have plotted out the various combinations of the different bacterial groups (hemolyzers, staphylococci, pseudodiphtheria), but there does not appear to be anything consistent or suggestive in the combinations to indicate anything of practical value.

In the six cases failing to give streptococci in culture the lesions were of long duration.

CONCLUSIONS

With proper precautions and under proper conditions streptococci may be obtained from nearly all cases of impetigo. If the full complement of streptococci is to be obtained on culture, it is necessary to take the material from an early and unerupted lesion. If this is not possible, it should be taken from the deep, redder parts from which all crusts have been removed.

Accepting as we do the conclusions of previous workers that impetigo is caused by streptococci, at least four different strains are concerned: *Streptococcus pyogenes*, *Streptococcus anginosus*, *Streptococcus subacidus* and *Streptococcus fecalis*.

Associated organisms, such as staphylococci, pseudodiphtheria bacilli, etc., are either extraneous or secondary invaders.

Streptococcus fecalis is not the factor in America that it was in Flanders, and there is little likelihood that it has been recently imported.

It cannot be predicted from the aspect of the clinical lesion (bullous, crusted or ecthymatous) what strain of streptococcus will be found on culture.

THE VIABILITY OF RINGWORM FUNGI IN DRY CUTANEOUS MATERIAL *

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This experiment was conducted to determine in a general way how long these fungi could remain viable in the surplus scrapings, hairs, etc., which had been preserved dry for future use in paper envelopes in our laboratory files. The results would also yield some rough idea of how long the material might retain its infectiousness in those articles of clothing (slippers) and the toilet (brushes and combs) which are not always periodically cleansed.

The material consisted of hairs, crusts and scrapings in which, as a routine, fungous elements had already been demonstrated in potassium hydroxid solution as the clinical case presented. The surplus material was preserved in black photographic paper, enclosed in a white paper envelope and filed in a small drawer. Only a few specimens had been determined culturally. Plantings were made without previous alcoholization on Sabouraud's proof agar and without the addition of any restrainer.

The table shows the scope of the tests and the results:

RESULTS OF TESTS

	Number of Cases Exam- ined	Number of Cases Giving Positive Culture	Percent- age Positive	Remarks	Negative Results
Tinea capitis.....	7	2	29	M. lanosum viable 424 days; uniden- tified fungus viable 312 days	Material 354, 585, 664, 665 and 677 days old
Tinea cruris.....	9	3	33	Epidermophyton inguinale viable 145, 174 and 433 days	Material 173, 354, 394, 395, 673 and 683 days old
Favus.....	1	0	0	Material 369 days old
Tinea corporis..... (circinata)	6	0	0	Material 244, 311, 410, 458, 640 and 684 days old
Tinea unguium.....	2	1	50	Unidentified fungus viable 418 days	Material 180 days old
Totals.....	25	6			
Average.....	25		

* From the Laboratory of Dermatological Research, Department of Cutaneous Medicine, University of Pennsylvania.

COMMENT

The six cases of tinea corporis (circinata) yielded no cultures.

Three of the six successful growths were viable after 400 days (*E. inguinale*, *M. lanosum* and the unidentified fungus in the case of *Tinea unguium*).

One third of the epidermophyton cases were viable after more than five months. This explains the occasional clinical recurrences and indicates that the clothing should receive attention in unusual recurrent cases.

Viability was lost in the older specimens. There was no growth in the group of eight samples over 500 days old.

While the tenacity of life of some of these cutaneous fungi is remarkable, in general it is within definite bounds, should not be over-rated, and cannot compare with that of our commoner saprophytic fungi like *Penicillium glaucum*, or many of the spore-bearing bacteria. In this connection it seems proper again to refer¹ to Dold's² work in China. He tested four lots of tinea cruris scales (which had been kept in sterile envelopes) at several intervals. One lot failed to grow after twelve days, three after twenty days, and none grew after thirty days. As far as I am aware, difference in strains³ has not been established for *Epidermophyton inguinale* to account for such variance in resistance as is shown by Dold's and my own work, nor does there appear to be any difference in the method of preserving the scales to account for the variability.

1. Farley, D. L.: The Cultivation of *Epidermophyton Inguinale*, Arch. Dermat. & Syph. **2**:466 (Oct.) 1920.

2. Dold, Herman: China M. J. **34**:34 (Jan.) 1920.

3. Wende, G. W., and Collins, K. R.: A Contribution to the Study of *Epidermophyton Inguinale*, Arch. Dermat. & Syph. **3**:1 (Jan.) 1921. Black-gray and yellow types are described by these authors, but have not been confirmed. They also mention (p. 10) peculiar color changes in different subcultures ranging through gray, green, salmon-pink, grayish green and mouse-gray. In a personal communication Dr. Fred D. Weidman tells me that he has seen fructifications in contaminants which resemble those figured by these authors, and that from these and the descriptions he feels sure these "types" are separate species from *Epidermophyton* and are contaminants.

SYPHILITIC BACKACHE

A SYMPTOM OF SYPHILIS OF THE SPINAL CORD, LUMBAR
MUSCLES AND VERTEBRAE WITH REPORT OF CASES *

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Among the many causes of backache, syphilis should be considered. Although backache of syphilitic origin is, in the majority of cases, a symptom of neurosyphilis, nevertheless, the subject may be more properly discussed by classifying backache as a symptom of syphilitic involvement of the spinal cord, lumbar muscles and vertebrae.

BACKACHE DUE TO SPINAL CORD SYPHILIS

Backache of syphilitic origin is in most instances a symptom of spinal cord syphilis. In this condition the underlying pathology is meningeal. The neurologic sensations are in reality produced by irritation of the posterior sensory roots, and these are irritated in turn by the thickened and inflamed cord membranes through which they pass. Although clinically it is impossible to determine whether these root symptoms are caused by a root neuritis which is independent of the meningitis or by the meningitis and its consequent effect on the roots, as a matter of pathologic observation, rarely, if ever, isolated involvement of either the roots or cord occurs, although frequently a disproportion exists between the involvement of the spinal roots and the cord itself.

A root neuritis may arise in other ways. The roots may be compressed by the specifically inflamed membranes, or the inflammation may extend from the membranes into the roots themselves. In this way the individual nerve fibers are secondarily involved. Inflammation may also arise from the specifically diseased vessels. In addition to these forms of involvement, gummas may become localized in the roots. In very rare instances, a root neuritis may arise from a syphilitic periostitis of the vertebrae.

In a specific meningitis involving the cord, the posterior surface is not only more frequently involved than the anterior surface, but the meningitis is more extensive and more intense in this region. It is usually most severe in the dorsal region, since there the spinal cord has the least resistance.

* Read before the College of Physicians and Surgeons, Section on General Medicine, Philadelphia, Oct. 25, 1920.

A syphilitic spinal meningitis may be acute, subacute or chronic, and may be present from the exanthematous period of the disease until many years later. The headache and backache encountered in the acute secondary period of syphilis are frequently meningeal in origin. This was recognized prior to the introduction of lumbar puncture by Quinke in 1891. Notably, Lang, in 1880, and others referred to these, as well as to other symptoms, as arising from spinal meningeal irritation, and pointed out that occasionally the meningeal irritation passes into a meningitis. In the light of present knowledge arising from spinal fluid examination in the acute stage of syphilis, we know that the spinal fluid at this time frequently shows a varying degree of abnormality, which doubtless manifests the severity of meningeal involvement to which the older writers referred.

Backache, a symptom of spinal cord syphilis, is usually a part of the meningeal syndromé. The meningeal symptoms, in general, are essentially the same as in the other forms of meningitis. These symptoms are: pain, which may exist between the shoulders or in the back, paresthesias, painful sensations and acute attacks of girdle pain, which radiates anteriorly around the lateral part of the chest. Hyperesthesia is present, and the tendon and skin reflexes are increased. Some writers (Erlenmeyer, Siemerling, Oppenheim and Lang) have emphasized the variability of the patellar reflexes. They are alleged to vary from an entire absence to an increase in short periods of time from day to day, or longer. The explanation given for this is the variation in swelling of the syphilitic infiltrated tissue which compresses the fibers which are responsible for the patellar reflexes.

It is frequently mentioned, first perhaps by the older French syphilologists, that the pain, as heretofore noted, is worse at night. Indeed, this has been stated in reference to other forms of syphilitic pathology. This statement has apparently been copied from textbook to textbook and, in my experience, so far as present day syphilitic pathology is concerned, this tautology does not constitute reality. In addition to these sensory irritative symptoms, there are also symptoms of motor irritation in the form of tension in the musculature, which may increase the contractions. Backache, stiffness and tiredness are the chief complaints of the patient. One finds clinically a rigidity of the back, combined with a localized or diffuse tenderness to percussion of the vertebral column. In addition, movement may be painful.

This syndrome may exist in a varying degree and for a long period of time. The clinical picture may be modified by an extension of the pathologic condition to the cord proper. The pathologic lesions may be numerous and disseminated, and the clinical picture is therefore a variable one. Indeed, further discussion would involve a discussion of

the subject of cerebrospinal syphilis. However, it may be mentioned that after the pathologic process has attacked the conduction tracts, symptoms of sensory and of motor involvement will of necessity follow, and the additional clinical features of meningomyelitis supervene.

In many of the cases under consideration, besides the objective symptoms of neurosyphilis already mentioned, evidence of involvement of other portions of the neuraxis may be present. An isolated involvement of the spinal cord in syphilis is exceptional, considerably more so pathologically than clinically. Fournier reports more than five times as many cases of cerebrospinal syphilis as the pure spinal type. Erb states that in his experience spinal cord syphilis of the nontabetic type occurs only one tenth as often as tabes.

The response to antisypilitic therapy in these cases is proportional to the acuteness and duration of the pathologic process. The result of treatment and the prognosis are worse when the condition has progressed to irreparable secondary changes in the cord. An appropriate plea can therefore be made for a thorough history and examination of every syphilitic in order that treatment may be administered in the meningeal stage of neurosyphilis. The presence of a negative blood Wassermann reaction in this class of case would not be remarkable. If this laboratory evidence is taken as a criterion of the status of the syphilitic infection, and important subjective and objective evidence of syphilitic involvement of this part of the neuraxis, which is relatively not a silent one, is not searched for, it may insidiously progress to a parenchymatous involvement. The spinal fluid in these cases is always positive. The pleocytosis in a measure depends on the severity of meningeal involvement. The Wassermann reaction may be positive in both high and low dilutions of spinal fluid. The colloidal gold reaction shows changes in the nature of a syphilitic curve.

Cases 1, 2 and 3 are illustrative of backache due to spinal cord syphilis.

BACKACHE DUE TO SYPHILIS OF THE LUMBAR MUSCLES

Under the heading of muscle involvement may be placed the backache which may be present in the acute secondary stage of syphilis. In this stage, it is either meningeal in origin, or a toxic expression of the acute spirochetemia. In the latter instance, it is part of the malaise present in the rather severe acute cases. It may be the chief complaint of the patient and may appear for some time prior to the secondary eruption. There is backache of this description in Case 4. The patient complained of malaise, headache and backache of several weeks' duration. When first seen, he was obviously sick—the temperature ranged from 102 to 105 F., for the first three days, and from 104 to 106 the

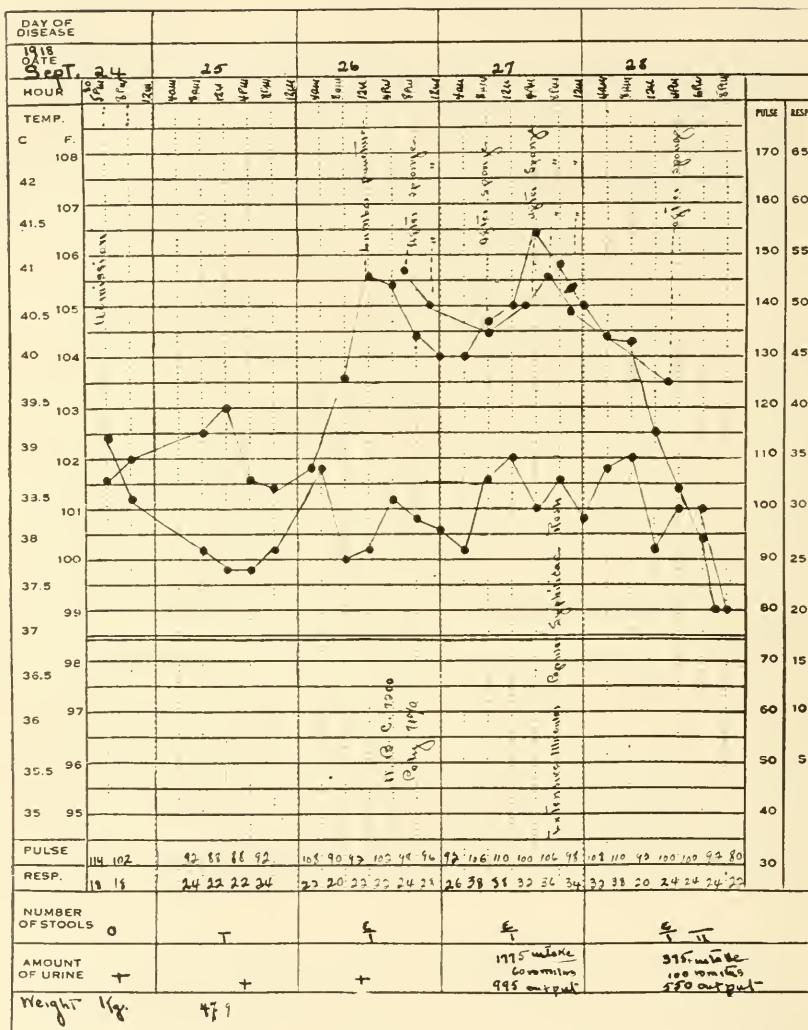


Fig. 1.—Temperature curve in Case 1 of acute secondary syphilis. Within thirty hours after the appearance of the eruption, the temperature dropped from 106.5 F. to 99 F. This fall in temperature by crisis after cutaneous manifestation is characteristic of the fever in acute secondary syphilis.

following twenty-four hours (Fig. 1). It is of interest to note that on the appearance of the diffuse maculopapular syphilid, the temperature dropped by crisis to normal. An internist, who saw the patient prior to the appearance of the eruption, made a tentative diagnosis of typhoid fever. This disease was rightly suspected from the history, the appearance of the patient, the temperature curve, the relatively lowered pulse rate, the enlargement of the spleen and the blood picture. In addition, a few scattered, faint macular lesions suggested the roseola of typhoid fever. These lesions were early appearing macular syphilids. Although some of the characteristic symptoms of typhoid fever were lacking, this would not have precluded the diagnosis of typhoid since the clinical picture of the disease is not always definite. The case is an instance of the simulation of typhoid fever by acute secondary syphilis.

In view of the negative spinal fluid in Case 1, it may be pointed out in passing that lumbar puncture, performed in the acute untreated stage of syphilis, is not without untoward consequences, that is, if the puncture is faulty and blood is obtained. This statement is based on experimental knowledge that blood, as well as other substances, when injected into the spinal fluid, acts as an irritant to the meninges and apparently causes a definite let-down in the meningeal-choroidal barrier between the blood and spinal fluid. In this way it is possible experimentally to infect the neuraxis with an infection from the blood. Indeed, simple lumbar puncture may constitute such an irritant. This possibility has been demonstrated by the work of Flexner and Amos¹ on poliomyelitis, Weed² and his associates on streptococcic infection in cats, and by Mehrtens and MacArthur's³ studies of the arsenical content of the spinal fluid after various methods of treatment.

Backache due to syphilis may rise through syphilitic involvement of the lumbar muscles, although these muscles are not the ones commonly involved. However, it is possible for syphilis to involve any group of muscles.

Very little has been added to our clinical knowledge of syphilitic disease of the muscles since its first recognition by Theodosius in 1553. Excluding the muscles of the tongue and heart, syphilitic involvement of the muscles is rare.

1. Flexner, S., and Amos, H. L.: The Relation of the Meninges and Choroid Plexus to Poliomyelitic Infection, *J. Exper. Med.* **25**:525 (April) 1917.

2. Weed, L. H.; Weyeforth, Paul; Ayer, J. B., and Felton, L. D.: The Production of Meningitis by Release of Cerebrospinal Fluid, *J. A. M. A.* **72**:90 (Jan. 18) 1919.

3. Mehrtens, H. G., and MacArthur, C. G.: Therapy of Neurosyphilis, Judged by Arsenic Penetration of Meninges, *Arch. Neurol. & Psychiat.* **2**:369 (Oct.) 1919.

Backache, and indeed myalgia in other parts, occurring in the acute stage of syphilis, is more likely a toxic expression of the acute spirochetemia, than a myositis.

Comparatively early in the infection, a diffuse interstitial myositis may appear. This condition may affect any muscle but particularly one of the flexors and especially the biceps. It is insidious in onset and characterized by pain, which usually develops concomitantly with contraction and swelling of the muscle. The patient complains of pain and inability to straighten the joint. The muscle is tender and feels firm and thickened, and an attempt actively to straighten the joint causes pain. Such an involvement is seen in Figure 2. Later in the disease, the commoner form of syphilis of the muscle, a gumma, may form



Fig. 2.—One type of syphilitic myositis involving the biceps. The history of syphilitic infection was negative. The involved muscle was swollen, painful on motion and tender to the touch. The onset was gradual and apparently causeless; other clinical evidences of syphilis were present. The blood Wassermann reaction was $++++$. After antisyphilitic therapy all subjective and objective symptoms disappeared. No local treatment was applied.

in one or more muscles. Those usually involved are the muscles of the arm and leg. The involvement may be localized or generalized or a combination of the two forms. In the localized form, a firm infiltration, accompanied by pain, occurs within the muscle.

The gummatous masses may break through the skin, resulting in an ulcer, or they may retrogress, causing a contracted or shrunken muscle. In the generalized form, there are pain and swelling of the muscle, which is firm to the touch. The muscle may become adherent to surrounding structures, causing impairment of motion. When the two

forms are combined, individual gummas are palpable and the muscle becomes uneven in places and shortened; at other points, the gummas may break down, causing ulceration and suppuration. Rarely the whole process ends in calcification and ossification.

BACKACHE DUE TO SYPHILIS OF THE VERTEBRAE

Although syphilis frequently involves the osseous system, notably the skull, clavicle and tibia, it rarely involves the vertebrae. Syphilitic involvement of the vertebrae is most often seen in the cervical region. Indeed, some writers view with skepticism its alleged occurrence in the dorsal and lumbar regions. Many of the reported cases of syphilis of the vertebrae have been mistaken for tuberculosis, and Leyden ⁴ rightly states that the diagnosis of syphilitic vertebral exostosis has been too lightly made. However, there have been reported a number of authentic cases of syphilis of the vertebrae, including the dorsal and lumbar regions, in which the diagnosis was confirmed at necropsy.

In 1904, Neumann ⁵ analyzed fifty-five cases, which he collected from the literature. The cervical region was involved in 65 per cent. of the cases, and the dorsal and lumbar regions in 31 per cent. Ziesche, ⁶ in 1911, analyzed a total of eighty-eight cases reported in the literature. The cervical region was involved in 69 per cent. of the cases and the dorsal and lumbar regions in 23 per cent. In 1915, Hunt ⁷ reviewed the subject, with a report of four cases, which made a total of 100 authentic cases reported in the literature.

The cervical region is more frequently involved because of its proximity to the cranial bones, resulting in an extension of the disease from this region. The cervical vertebrae may also become involved through a direct extension from pharyngeal gummas.

Unlike tuberculosis, syphilis is more likely to affect the spinous and transverse processes than the bodies of the vertebrae. Pathologically, such involvement is seen as a periostitis and osteitis, which may progress to necrosis and sequestration of bone. There is considerably less likelihood of pus formation with the development of a "cold abscess," as seen in tuberculosis of the vertebrae.

In the symptomatology of this disease, there is no characteristic symptom which serves to distinguish it from other pathologic condi-

4. Leyden, E.: Ueber ein Fall von syphilitischer Wirbelerkrankung, *Berl. klin. Wchnschr.* **26**:461-462, 1889.

5. Neumann, I.: Ueber syphilitischen Erkrankungen der Wirbelsäule, *Wien. med. Presse* **45**:14-19 (bibliography), 1904.

6. Ziesche, H.: Ueber die syphilitischen Wirbelentzündung, *Mitt. a. d. Grenzgeb. d. Med. u. Chir.* **22**:357-388 (bibliography), 1910-1911.

7. Hunt, J. R.: Syphilis of the Vertebral Column, *Am. J. M. Sc.* **148**: 164-179 (bibliography), 1914.

tions of the spine. The onset may be acute, or chronic. Pain is the predominating symptom. It may be dull and confined to the involved vertebrae, or acute and lancinating, following the distribution of the secondarily involved nerve roots. A secondary involvement of the spinal cord and its membranes occurs less frequently than an involvement of the brain from disease of the skull. Hunt states that neural complications occurred in 25 per cent. of the 100 cases reported in the literature up to 1915.

Some writers say that the pain is worse at night. On examination, tenderness and rigidity are found to be present over the involved area and there is obliteration of the normal vertebra curve. Deformity may

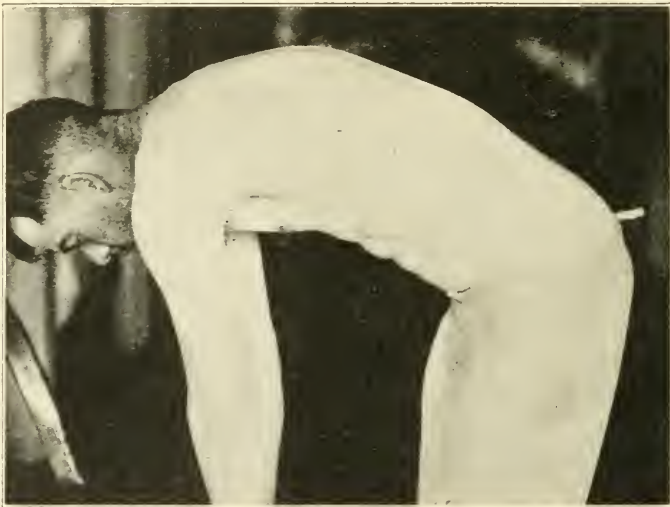


Fig. 3 (Case 5).—Obliteration of the dorsolumbar curve. Roentgenographic examination revealed necrosis of the body of the fifth lumbar vertebra, which was probably tuberculous, the symptoms of which appeared after syphilitic infection.

occur, which, when present, is consistent with the degree of pathologic involvement.

The differentiation of syphilitic involvement of the vertebrae from tuberculosis is, in some cases, difficult. The foregoing considerations are differential features. The roentgen ray is a valuable means of establishing a differential diagnosis. Indeed, in most cases it is the only way in which a diagnosis can be made.

If backache in a syphilitic is due to some pathologic involvement of the lumbar vertebrae, it is considerably more likely to be tuberculous than syphilitic. This is particularly true if syphilis has been recently acquired, since this disease is likely to activate latent tuberculosis. The

association of the two diseases is a very baneful one. Sergent⁸ presents considerable clinical evidence to show that syphilis plays an important part in the causation of tuberculosis in its many clinical manifestations. In this regard I may appropriately recall the following statement of Landouzy: "La syphilis fait le lit de la tuberculose," and that of Fournier, who stated that he would not hesitate to inscribe syphilis in the etiologic chapter of pulmonary tuberculosis.

In view of these considerations it becomes apparent how easily tuberculosis of the vertebrae, existing in a syphilitic, can be mistaken for syphilis.

Improvement following antisyphilitic treatment does not prove the syphilitic nature of the pathologic condition, since tuberculous lesions in a syphilitic are frequently improved after such treatment. Such an instance is seen in Case 5 (Fig. 3) of a man, recently infected with syphilis, who complained of backache. There were tenderness and rigidity of the lower lumbar region, and the roentgenogram disclosed necrosis of the body of the last lumbar vertebra. The appearance suggested tuberculosis, rather than syphilis. The backache improved following treatment with arsphenamin, mercury and iodid.

Nonna⁹ reports cases of vertebral necrosis in syphilitics, the subjective symptoms of which disappeared following antisyphilitic therapy. However, later the patients died of pulmonary tuberculosis, and necropsy demonstrated the vertebral involvement to be tuberculous in nature.

BACKACHE DUE TO SYPHILITIC SYNOVITIS OF THE SPINAL JOINTS

In addition to a syphilitic involvement of the vertebrae, backache may be caused by a synovitis of the spinal joints. This involvement is perhaps the commonest lesion in syphilis of the spine. Indeed, Whitney and Baldwin¹⁰ have frequently observed its presence in syphilitics. In their series of 100 syphilitics examined for joint lesions, with special reference to the condition of the spine, they observed twenty-six patients with normal spines. Six patients presented doubtful findings, the remaining sixty-eight patients presented spinal abnormalities of some kind; of these, all but four were of a type which they considered more or less characteristic of syphilis.

A syphilitic synovitis occurs relatively early in the disease, although the deformity and stiffness it produces doubtless remain indefinitely.

8. Sergent, Emile: *Syphilis et Tuberculose*, Paris, Masson et Cie, 1907; *Presse méd.* **16**:657 (Oct. 14) 1908.

9. Nonna, Max: *Syphilis and the Nervous System*, Ed. 2, Philadelphia, J. B. Lippincott Company, 1916, p. 228.

10. Whitney, J. L., and Baldwin, W. I.: *Syphilis of the Spine*, J. A. M. A. **65**:1989 (Dec. 4) 1915.

Usually three or four vertebrae are affected, although the process may attack more, indeed the whole dorsal region. Pain and backache are not prominent symptoms but rather deformity, localized stiffness and hypotonicity of the uninvolved spine, pelvic and hip joints. Roentgen-ray examination of the spine in this condition is negative.

The syndrome of this process as described by Whitney and Baldwin is as follows: Deformity when present consists of a prolongation of



Fig. 4.—Syphilitic synovitis of the spinal joints, showing hypotonicity and obliteration of the normal dorsolumbar curve.

the dorsal curve into the dorsolumbar region, where normally there is a concavity, or a flattening. There is a localized stiffness, at first due to spasm, and later to adhesions. Hypotonicity of the ligaments and muscles of the sacro-iliac joints and of the hips is a predominating symptom. This is manifested by the ease with which the patient can place the palms on the floor with knees straight (Fig. 4). This symptom is more marked in the cases of neurosyphilis. It is interpreted by Whitney and Baldwin as a sign of syphilis rather than as a sign of tabes, which is the usually accorded interpretation.

The two symptoms, localized stiffness and hypotonicity, are regarded by Whitney and Baldwin as almost pathognomonic of syphilis. One patient, a syphilitic (Fig. 4) presented the foregoing symptoms of syphilitic synovitis of the spine. She complained of backache. There was obliteration of the normal spinal curve with areas of restricted mobility, together with a marked degree of hypotonicity which is well shown in the illustration. The blood Wassermann was + + + +. There was no clinical evidence of neurosyphilis although the spinal fluid was not examined. A roentgen-ray examination of the spine was negative.

REPORT OF CASES

BACKACHE—SPINAL CORD SYPHILIS

CASE 1.—History.—A man, aged 48, gave a history of a genital lesion twenty years before for which only local treatment had been received. He had been married twelve years. His wife was living and was said to be well. There were no living children, although there had been a stillbirth ten years before, but there had been no miscarriages. The chief complaint was constant backache, of from three to four years' duration, localized in the lower lumbar region. He had been treated by many physicians. He complained also of headache. There were no other subjective symptoms of neurosyphilis.

Physical Examination.—This disclosed nothing of any importance excepting leukoplakia of the buccal mucous membrane.

Neurologic Examination.—The pupils were unequal, irregular in contour, and reacted sluggishly to light. The patella reflexes were exaggerated. The blood Wassermann reaction was + + + +. The spinal fluid contained 56 lymphocytes per c.mm.; globulin was positive, and the Wassermann reaction with 0.8 c.c. was + + + +. The colloidal gold reaction was 0013321100.

Treatment.—After arsphenamin and mercurial treatment, the backache improved. It finally disappeared during the continuation of treatment.

CASE 2.—History.—A woman, aged 38, who had been married thirteen years, had lost one child at the age of 3 months; there had been no miscarriages. Salpingo-oophorectomy had been performed nineteen years before. The chief complaint was backache, which had been persistently present for the last eight months. The backache involved the lower lumbar and sacral region, and at times there were sharp shooting pains radiating anteriorly around the lower costal areas. She had had headache for about the same period of time.

Neurologic Examination.—The pupils were irregular and unequal. Light and accommodation reflexes were absent in the right eye. The left eye reacted to accommodation, but did not react to light. The biceps, triceps and patellar reflexes were exaggerated. There was no Babinski sign or ankle clonus. There were no sensory disturbances and no paralysis. She had good sphincter control. The blood Wassermann reaction was + + + +. The spinal fluid contained 100 lymphocytes per c.mm.; globulin was positive, and the Wassermann reaction with 0.8 c.c. was + + + +. The colloidal gold reaction was not made.

Treatment.—Following the administration of arsphenamin, mercury and potassium iodid, there was considerable improvement of subjective symptoms.

CASE 3.—History.—A woman, aged 32, had been married sixteen years. Her husband was living and alleged to be in good health. There were two living

children. She had had three miscarriages. Her chief complaint was acute spasmodic pain in the sacral and right gluteal regions. These had been of sudden onset two weeks before with acute stabbing pains in the right hip which radiated downward over the gluteal region into the thigh. She had had backache for some weeks. At times she experienced paresthesia in the lower extremities.

Neurologic Examination.—The pupils were equal and regular in size and reacted to all reflexes. The patellar reflexes were exaggerated. There was no ankle clonus or Babinski reflex. She had good control of the sphincters. There was no loss of muscular power. The blood Wassermann reaction was + + + +. Spinal fluid examination revealed 125 lymphocytes per c.mm. The globulin was positive, and the Wassermann reaction with 0.8 c.c. was + + + +. The colloidal gold reaction was not made.

Treatment.—The subjective symptoms entirely disappeared following anti-syphilitic treatment.

BACKACHE—ACUTE SECONDARY SYPHILIS

CASE 4.—*History.*—A Filipino, aged 24, gave a history of headache, backache, arthralgia, and malaise of about three weeks' duration. He had had a genital lesion for from five to six weeks.

Physical Examination.—The patient was frail, underweight and obviously sick. The mouth, teeth and tongue were negative. The throat was congested. Examination of the heart and lungs disclosed nothing of any importance. There was enlargement of the lymph nodes, excepting the epitrochlear and occipital. Examination of the abdomen disclosed an enlargement of the spleen. There were a few scattered macular lesions suggestive of the roseola of typhoid fever. The bones and joints were negative. There was a lesion on the shaft of the penis, which was ulcerated, nonindurated and crusted. The temperature and pulse curves are given in Figure 1. A tentative diagnosis of typhoid fever was made pending laboratory studies.

Laboratory Examination.—Blood culture was negative. The Widal test was negative. Blood count revealed: leukocytes, 7,200, and polymorphonuclears, 71 per cent. The urine contained a trace of albumin and granular cysts. Dark-field examination of the genital lesion was negative. The patient had previously applied calomel. Dark-field examination of macular lesions was positive. The serum Wassermann reaction was + + + +. Spinal fluid examination revealed: cells, none; globulin negative; Wassermann reaction with 1 c.c. negative, and colloidal gold reaction 0011100000.

From the laboratory findings and subsequent clinical observation, the diagnosis of secondary syphilis became obvious.

BACKACHE—VERTEBRAL NECROSIS, SYPHILITIC (?)

CASE 5.—*History.*—A man, aged 26, with no history of tuberculosis in the family, gave a negative history, excepting for a chancre three years before which was followed by a secondary eruption. At that time, he received one injection of neo-arsphenamin and mercury by mouth for the following year. He had had no further treatment and no subjective symptoms until three months before, since which time he had been complaining of backache. The backache was of the nature of a dull localized pain in the lower lumbar region. It was worse when he was on his feet. He had no other complaint.

Physical Examination.—There was no evidence of pulmonary tuberculosis and no neurologic abnormality. There was a scar on the penis, and a gen-

eral adenopathy. Muscular rigidity was present in the lower lumbar region and there was an obliteration of the normal dorsal and lumbar curve (Fig. 3). There was tenderness on percussion of the lower lumbar vertebrae. Pain was present on jarring. The blood Wassermann reaction was + + + +. A roentgenogram of the lower lumbar vertebrae disclosed a necrosis of the body of the fifth vertebra, with considerable involucrum formation on the right. The roentgenogram suggested tuberculosis rather than syphilis.

SUMMARY

Syphilitic backache is classified as a symptom of syphilitic involvement of the spinal cord, lumbar muscles and vertebrae. In the majority of instances, it is a symptom of spinal cord syphilis.

Syphilitic backache, a symptom of syphilis of the spinal cord, is meningeal in origin and due to irritation of the posterior sensory roots. This involvement may be acute, subacute or chronic, and may be present from the exanthematous period of the disease until many years later. The symptom backache is a part of the meningeal syndrome. These symptoms in general are essentially the same as those in other forms of meningitis: pain, which may exist between the shoulders or in the back, paresthesias, painful sensations and acute attacks of girdle pain which radiate anteriorly around the lateral part of the chest. Hyperesthesia is sometimes present, and the tendon and skin reflexes are increased. In addition, there are symptoms of motor irritation. Backache, stiffness and tiredness are the chief complaints of the patient. Clinically, in addition to these neurologic abnormalities, there is rigidity of the back, combined with localized tenderness on percussion of the vertebral column. Other objective evidences of neurosyphilis are usually present, since an isolated involvement of the spinal cord is exceptional.

The usual spinal fluid findings in this condition are given. Case histories illustrating this type of syphilitic backache are presented.

A plea is made for a thorough history and clinical examination of every syphilitic in order that treatment may be administered in the meningeal stage of neurosyphilis rather than in the parenchymatous stage.

Backache Due to Syphilis of the Lumbar Muscles: The backache which is sometimes present in acute secondary syphilis is placed under this heading, although it is a toxic expression of the acute spirochetemia rather than syphilitic myositis. Syphilis of the muscles is discussed and various clinical types are presented.

Backache Due to Syphilis of the Vertebrae: A syphilitic involvement of the vertebrae is usually seen in the cervical rather than in the lumbar region. A brief review of the literature of syphilis of the vertebrae is given.

Syphilis is more likely to affect the spinous and transverse processes than the bodies of the vertebrae. The pathology of this condition is given. "Cold abscess" formation, which is usually present in tuberculosis, is considerably less likely to be encountered in syphilis.

In the symptomatology of this process there is no characteristic symptom which serves to distinguish it from other pathologic conditions of the spine. A secondary involvement of the spinal cord and its membranes is less likely to occur in syphilis than in tuberculosis.

The Differential Diagnosis of Syphilis of the Vertebrae: Syphilis may activate latent tuberculosis. This possibility must be considered in the presence of a pathologic involvement of the vertebrae in a syphilitic. The therapeutic test in these cases is not conclusive since tuberculous lesions in a syphilitic are improved after antisyphilitic treatment. A case history is given in which the necrosis of the lumbar vertebrae was probably tuberculous rather than syphilitic.

Backache may also be caused by a synovitis of the spinal joints. This involvement is the commonest lesion in syphilis of the spine. The syndrome of the process is this: Deformity, when present, is seen in a prolongation of the dorsal curve into the dorsolumbar region, where normally a concavity exists, or a flattening. There is a localized stiffness, at first due to spasm, and later to adhesions. Hypotonicity of the ligaments and muscles of the sacro-iliac joints and hips is a predominating symptom.

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XXIII.—IMMUNITY STUDIES IN EXPERIMENTAL SYPHILIS

INFECTIVITY AND SURVIVAL OF SPIROCHAETA PALLIDA IN RABBITS,
WITH OBSERVATIONS ON SOME STRAINS FROM LATENT SYPHILIS

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Local immunity, or a better term, resistance to reinoculation in syphilis has been established as a fact both experimentally and clinically. Information is lacking with regard to the behavior of *Spirochaeta pallida* which have been exposed to such influences as might logically be assumed to modify the course of an infection in the animal body. It has been shown in a previous study¹ that syphilis in man, when latent and outwardly inactive, can be associated with the presence of *Spirochaeta pallida* in the glands and in the semen. In the experimental animal this question has been approached as a control on the problem in man, and results, such as localization in certain glands and preliminary observations bearing on latency in experimental syphilis, have been recorded in another place.² The brilliant studies of Brown and Pearce³ which were made in connection with the therapeutic action of drugs have supported such findings independently. All phases of the problem which deal with cyclic changes in the course of infection in syphilis, the regression of lesions and the factors tending toward and modifying a condition known as latency, are intimately linked with the wider and more fundamental aspect of immunity. Whatever knowledge is to be gained from a study of the behavior of different strains of *Spirochaeta pallida* in animals may find some application to the

* Work done under a grant from the U. S. Interdepartmental Social Hygiene Board, Washington, D. C.

* Studies, observations and reports from the dermatological department of the Barnard Free Skin and Cancer Hospital and the Washington University School of Medicine, St. Louis, Mo., U. S. A., service of Drs. M. F. Engman and W. H. Mook.

1. Ebersson, F., and Engman, M. F.: An Experimental Study of the Latent Syphilitic as a Carrier, J. A. M. A. **76**:160 (Jan. 15) 1921; Engman, M. F., and Ebersson, F.: XXI.—A Biologic Study of Latency in Syphilis, Arch. Dermat. & Syph. **3**: Pt. 1, 347 (April) 1921.

2. Ebersson, F.: Dissemination of *Spirochaeta Pallida* in Experimental Syphilis, Arch. Dermat. & Syph. **3**:111 (Feb.) 1921.

3. Brown, W. H., and Pearce, L.: J. Exper. Med. **31**:749 (June) 1920.

solution of the general problem. This paper represents, therefore, a report of certain findings which were incidental to the immunity studies now in progress.

There are certain difficulties involved in an attempt to study factors which may be likely to alter the virulence of an infectious organism. In the first place, we have no reliable criteria by which to measure the infective power of different strains of *Spirochaeta pallida*. If the incubation period is to be taken as a guide, then factors such as dosage, for example, must be subject to control and others be kept constant in order that results may be comparable. When, as in the case with syphilis in the rabbit, it becomes difficult to control certain fortuitous elements, the measure of accuracy is lessened considerably. Again, the difference in individual strains of spirochetes tends to confuse the picture so that the property of generalization, which some strains may possess, cannot be relied on for the degree of virulence. To make matters more complex, this manifestation seems to be influenced further by artificial procedures which are brought to bear on the primary focus of infection, as has been shown by Reasoner,⁴ and Brown and Pearce,⁵ and noted in our own studies.

ANIMAL PASSAGE AND ITS BEARING ON THE QUESTION OF VIRULENCE

The point of departure for the experiments which are embodied in the present report was the oft repeated opinion of most investigators that passage through animals enhances the virulence of *Spirochaeta pallida*. This idea was first promulgated by Uhlenhuth and Mulzer.⁶ Opposed to this view are the studies of Zinsser, Hopkins and McBurney,⁷ who found no apparent increase of infective power, although they admitted certain fluctuations due to factors in the technic which they employed. Reasoner,⁴ also, has stressed certain points which may modify the success of inoculation with material from syphilitic sources. However, with the exception of Brown and Pearce,⁸ investigators have ignored heretofore the possible importance of even a rough quantitative procedure in the determination of differences in virulence of strains which were used in the experiments. When it is desired to obtain successful "takes," a technic such as Brown and Pearce have described meets the requirements. For the purpose, how-

4. Reasoner, M. A.: Some Phases of Experimental Syphilis, J. A. M. A. **67**:1799 (Dec. 16) 1916.

5. Brown, W. H., and Pearce, L.: Arch. Dermat. & Syph. **2**:675 (Dec.) 1920.

6. Uhlenhuth, P., and Mulzer, P.: Arb. a. d. k. Gsndtsamte **44**:307, 1913.

7. Zinsser, H., Hopkins, J. G., and McBurney, M.: J. Exper. Med. **23**:329 (March) 1916.

8. Brown, W. H., and Pearce, L.: J. Exper. Med. **31**:475 (April) 1920.

ever, of studying the survival in vivo of strains taken from experimentally infected animals, further refinements are necessary, if the period of incubation is to be taken as an index of any value. Repeated passage of *Spirochaeta pallida* from animal to animal is a two-phase reaction. Adaptation to the host means the subjecting of spirochetes to such mechanisms of defense and biochemical reactions as may tend to reduce virulence rather than to increase it in response to locally developed immune substances or metabolic products. From the standpoint of latency, such factors have to be kept in mind, and it is a short step to the belief that spirochetes taken from old or receding lesions would tend to show longer incubation periods when transferred to other animals. This point has been observed irregularly in our study of behavior of strains of *Spirochaeta pallida*, and from the methods employed we are led to believe that inoculations made from lesions of different age are not correlated with prolongation or diminution of the incubation period. Different factors, such as the strain of spirochete and the technic used, may be of more importance. If the vitality of the spirochetes is diminished by residence within a zone of the testicle, the dose of virus used should have some effect on the speed of reaction, yet this is not generally the case, even when other factors are kept relatively constant. To follow up this conception it would be necessary to prove that distinct differences exist between different "lines of descent" obtained from a series of animals which represent transfers from actively developing lesions and a series of generations derived from animals with old, regressive lesions. Each new generation would include, therefore, in series, animals which had been inoculated with *Spirochaeta pallida* taken early and late in the course of infection. Any true variation of the incubation period and other points of interest can be discerned by such a procedure.

EXPERIMENTAL WORK

Organisms Studied.—Seven strains of *Spirochaeta pallida* were used in the experiments to be reported. Of these, three were isolated from the inguinal glands of patients having latent syphilis, two from the semen of similar patients, and two from penile chancres in active cases. The information to be gleaned from any one strain was substantially the same for all, so that two typical examples have been selected for illustration in this paper under the heading of infectivity and survival, while the differences which may appear to exist among *Spirochaeta pallida* from latent sources as compared with the others will be treated separately. These two strains, described as No. 137 and No. 170, have been isolated, respectively, from an inguinal gland of a latent syphilitic patient and from a penile chancre of a patient with an active case. They have been carried in rabbits in this laboratory for over eighteen months.

Animals Used.—Medium sized gray and brown rabbits with well developed testicles were used. As a rule, the animals were from 5 to 6 months old at the time of inoculation.

Technic.—Emulsions of *Spirochaeta pallida* were prepared from material taken directly from the lesion in the testicle by means of a finely drawn out capillary glass pipet. Warm salt solution was added in a small amount to the testicular puncture fluid which was expelled into a sterile Petri dish with the aid of a rubber nipple attached to the pipet. A sterile glass rod, flattened at one end, and bent at a convenient angle, was used to grind up the sticky mass in the smallest possible volume of solution. This was next drawn up into a pipet through a thin layer of sterile absorbent cotton placed in the homogenous emulsion. The perfectly clear fluid containing the organisms free from any tissue or foreign material was then ready for injection. The suspension of spirochetes was prepared so as to average about three for each field. The material was injected in amounts of 0.5 c.c. directly into the center of the testicle by means of glass Luer syringes fitted with a 21 gage needle, $\frac{5}{8}$ inch in length.

The rabbits were examined daily after two weeks had elapsed and sub-inoculations were made at different intervals from the same animal as well as from a single transfer from each rabbit of any series which represented the same new generation in each instance. By means of this method frequently repeated puncture of an individual lesion was avoided and more material for continuous transfer made available from those animals which had to be punctured repeatedly in order to keep the supply of animals at a minimum. Incidentally, the procedure made it possible in some degree to overcome whatever error may prevail in an attempt to exclude the withdrawal of *Spirochaeta pallida* from new minute lesions which may have become localized adjacent to an original old area in the testicle. The shortcomings of technic were appreciated in this connection, and an effort was made to eliminate all possible inaccuracy. Where some degree of metastasis or extension had occurred seemingly, care was taken to avoid any other than the old area which, as a rule, regressed *pari passu* with the age of the lesion. Results with both methods, carefully followed, revealed no essential differences and checked reasonably accurately.

INCUBATION PERIOD AND SURVIVAL WITHIN THE RABBIT TESTICLE

The persistence of *Spirochaeta pallida* in testicular lesions was marked by considerable variation. This variation did not seem to be associated with differences in the period of incubation, as reference to the correlation tables will show (Tables 1 and 2). Admitting the difficulty of proving the complete absence of organisms by the method of puncture and dark-field examination, a further procedure was resorted to, namely, that of inoculating new animals with emulsions of testicles which were found to be free from spirochetes. Especial effort was made to inject only clear fluid prepared in the manner described. In several instances, testicles which appeared to be normal after varying times subsequent to spontaneous disappearance of lesions, were used in this manner to determine relatively the ultimate period of survival. Excluding this group of animals for the present, the results in general may be summarized thus: *Spirochaeta pallida* could be demonstrated by puncture for periods ranging from one day to four and a half months

or more, irrespective of the period of incubation, which varied as much as seven weeks beyond that of the observed minimum, namely, from 18 to 20 days. No correlation seemed to exist between a short period of incubation and a rapid disappearance of organisms and the reverse (Tables 1 and 2). As far as could be determined, there were no

TABLE 1.—STRAIN 137. CORRELATION-AGE OF LESION, INCUBATION PERIOD, SURVIVAL *

Survival of <i>Spirochaeta Pallida</i> (in Days) in Testicle as Shown by Puncture	Age of Lesion or of Spirochetes in Lesion at Time of Subinoculation						
	...	000	000
1-5.....	...	000	+	000	+
6-10.....	0
11-15.....	++	++	0
16-20.....	..	0	0	+
21-25.....	+	00	+	0
26-30.....	..	+	..	+
31-35.....	+
36-40.....	+
41-45.....
46-50.....	0
51-55.....	..	0	+
56-60.....
61-65.....
66-70.....	+	0	+
76-80.....
90-100.....	+
120-130.....	+
Incubation period (days).....	18-25	26-33	34-41	42-49	50-57	58-65	66-75

* In Tables 1 and 2 the symbols indicate individual generations of the strain; 0, age of lesion at time of subinoculation; +, survival of *Spirochaeta pallida* in testicle; *, incomplete observations.

TABLE 2.—STRAIN 170. CORRELATION-AGE OF LESION, INCUBATION PERIOD, SURVIVAL

Survival of <i>Spirochaeta Pallida</i> (in Days) in Testicle as Shown by Puncture	Age of Lesion or of Spirochetes in Lesion at Time of Subinoculation										
	000	..	0	..	000	0	0	..	0
1-5.....	+	0	+	000	0	0	0
6-10.....	0	000	0	..	++	+	+
11-15.....	+	+	++
16-20.....	+	..	+	+	0
21-25.....	000	..	0	+	0
26-30.....	+	0	+	0	+	0
31-35.....	+
36-40.....	..	+	0	0
41-45.....	..	+	0	+
60-65.....	+	+	+
70-75.....	..	0	+
Incubation period (days).....	18-21	22-25	26-29	30-33	34-37	38-41	42-45	46-49	50-60	60-75	70-75

differences to be seen in any series of animals regardless of the number of passages of the strain or the age of the lesion at the time spirochetes were taken for subinoculation. These points are shown graphically in the tables which summarize the data of different "lines of descent" (Tables 3 and 4).

TABLE 3.—SUCCESSIVE GENERATIONS OF A STRAIN OF SPIROCHAETA PALLIDA
FROM A CASE OF LATENT SYPHILIS *

I. 137 50 26											
II. 198 37 19 1				II. 203 38 7(D) 4				II. 207 29 19 18			
III. 221 23 19 1											
IV. 256 21 11 1				IV. 262 35 38 16							
V. 244 69 2 9				V. 295 42 20 5				V. 296 38 53 5			
				VI. 325 46 14 20				VI. 282 80 44 124			
				V. 298 35 66 5				VII. 364 34 92 1			
				V. 299 24 10 7				VIII. 383 25 68 1			
				VI. 313 31 2 1				IX. 401 40 25 1			
				V. 239 33 21 5				IX. 414 28 21 18			
				V. 213 33 7 13				IX. 418 31(neg.) 32			
								VI. 305 34 10 124			
								VII. 340 46 127 1			
								VIII. 343 26 6 3			

* In Tables 3 and 4, the Roman numerals represent generations in rabbits' testicles and the figures, reading from left to right indicate, respectively, the number of the rabbits, the incubation period in that animal, the survival of *Spirochaeta pallida* as found by dark-field examination of puncture material from the testicle, and the age of the lesion or of spirochetes in such lesion at the time subinoculation was made. Figures in bold face type represent incomplete observations. D = death.

TABLE 4.—SUCCESSIVE GENERATIONS OF A STRAIN OF SPIROCHAETA PALLIDA
FROM CHANCRE IN PRIMARY SYPHILIS

I. 170 33 19											
II. 204 33 21 1						II. 210 34 7 18					
III. 220 30 12 1											
III. 245 26 19 (D) 20						IV. 260 21 14 3					
IV. 277 23 36 7						V. 288 25 6 9					
V. 300 37 9 23						V. 242 20 7 9					
V. 301 28 8 23						VI. 211 21 65 5					
V. 315 28 74 34						VII. 319 29 28 6					
VI. 223 30 43 38						VIII. 327 43 62 1					
						VII. 320 24 53 25			IX. 311 26 20 36		
						VIII. 235 70 10 1			X. 333 27 5 1		
						XI. 347 46 6 3					
IV. 148 20 42 19						XII. 373 20 36(D) 1					
V. 121 28 8 43						XIII. 395 23 52 10					
IV. 152 20 16 19						XIII. 387 22 60 1					
IV. 291 20 3 19						XIV. 417 28 14 28					
						XIV. 413 53(neg.) 10					

RELATION BETWEEN SPIROCHAETA PALLIDA FROM OLD LESIONS,
SURVIVAL IN TESTICLE AND INCUBATION PERIOD

Cyclic changes in testicular lesions have been noted in our series of experiments, and this phase of the study will not be considered here in view of the thorough analysis which has been given in the work of Brown and Pearce.⁹ Periodic fluctuations in the spirochetal content of lesions such as they have described seem to be associated regularly with syphilis in rabbits, as our own studies have demonstrated. Whether or not these cyclic changes go hand in hand with other factors is of importance primarily from the standpoint of possible differences in infectivity of organisms taken from lesions at different times when the incubation period and survival under a set of conditions may be compared.

The age of a lesion at the time transfers were made to new series of animals did not affect the period of incubation or the survival of spirochetes within the testicles of succeeding generations of rabbits. It would appear that *Spirochaeta pallida* assumes a condition of latency not devoid of its original infective properties. Furthermore, in several instances in which different amounts of organisms were used for inoculation, no departure from the norm was to be detected. These observations become more significant and more easily interpreted in connection with the protective properties of serums obtained during both the active and latent stages of experimental syphilis, a study which will be reported subsequently.

Spirochaetae pallidae were recovered for variable periods of time up to more than four and a half months when this paper was written. Subinoculations were made at intervals anywhere from one day to more than ten weeks after organisms were first demonstrated in the testicle. In Tables 5 and 6 are given some of the observations which show at a glance that no correlation exists between the age of the lesion or the spirochetal content of such lesions and the survival within the focus of infection. Whether or not the spirochetes which were used for inoculating new series of animals were fresh or old, did not appear to influence adaptation to the testicle as measured by survival, or to affect the period of incubation.

TYPES OF LESIONS

The syphilitic manifestations which were observed in the testicles of rabbits were, with certain exceptions, not constant for any of the strains used in this study. There were variations from a diffuse or interstitial orchitis to a circumscribed induration with all possible gradations

9. Brown, W. H., and Pearce, L.: J. Exper. Med. **31**:709 (June) 1920.

inoculation of the opposite testicle in the course of the infection. The development of scrotal chancres was observed on three occasions following intratesticular inoculation of the opposite testicle. One rabbit which had been inoculated with a strain in the seventh generation gave a positive reaction after an incubation period of thirty-four days. The lesion was confined to the upper pole of the left testicle and was

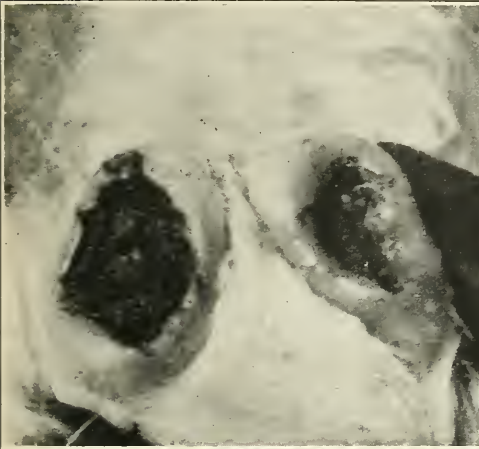


Figure 1

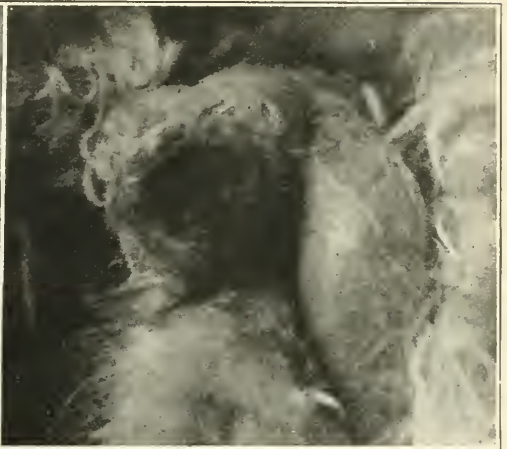


Figure 2

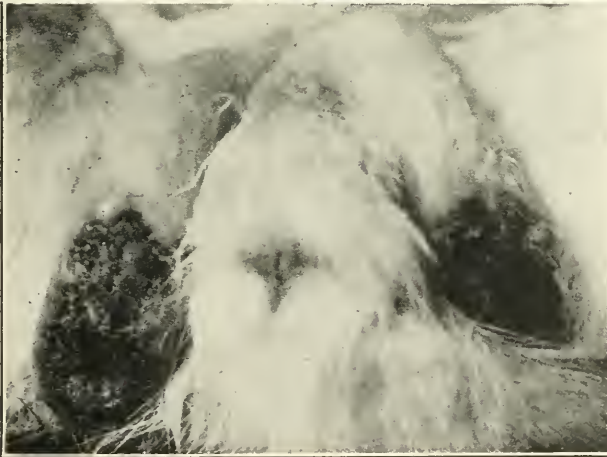


Figure 3

Scrotal infections in the course of active processes in opposite testicles.

nodular in type. Six weeks later a chancre, 1.5 by 3 cm., developed on the scrotum of the right testicle. Two weeks later, the originally infected testicle presented a chancre-like lesion immediately adjacent to the primary lesion (Fig. 1). The second example of this nature occurred in an animal which had been inoculated similarly with the strain of a like generation from another series. The original lesion in the left testicle first appeared as a circumscribed nodule nineteen days

after inoculation, and forty days later the right testis showed a scrotal chancre measuring 1 by 3 cm. (Fig. 2). A third instance of chancrous lesions with this strain occurred in the eighth generation which represented a subinoculation from the preceding animal just mentioned. A nodular lesion, developing after an incubation period of twenty-five days, was followed thirty-one days later by a scrotal chancre at the original site of infection. Ten days later a similar scrotal lesion occurred at the lower pole of the testicle. The fourth example of autoinoculation occurred in the fourteenth generation of a chancre strain. A nodular lesion developed at the upper pole of the left testicle twenty-three days after inoculation. Eight weeks later a scrotal chancre, 1 by 1.5 cm., was noted at the lower pole of the same testicle and on the right a chancre 1 by 2 cm. with an indurated border about 4 mm. in thickness (Fig. 3). The remaining two examples of this nature may be dismissed briefly with the observation that it is possible for a scrotal lesion to develop soon after the appearance of a lesion within the testicle, in fact, in one instance a primary manifestation appeared after twenty-eight days' incubation.

REINOCULATION EXPERIMENTS AND THE POSSIBLE INFLUENCE OF SENSITIZATION

The autoinoculations which have been mentioned and the well-known phenomenon of scrotal lesions occurring subsequent to intra-testicular injection of *Spirochaeta pallida* are suggestive of the possible importance which might be attributed to the sensitization of certain tissues in the animal body during active infection with syphilis. Our knowledge of the mechanism by which syphilitic gunmas are developed is indicative of a sensitizing process in which spirochetal cell-products or toxins play a part. In the rabbit testicle the purely local immunity of an infectious process is sharply defined by the manner in which new crops of lesions appear adjacent to involved areas. Chancre-like lesions, such as have been described in this paper and in the work of Brown and Pearce, seem to conform to a picture of necrosis and sloughing and, in general, to possess the characteristics of a true secondary manifestation. In a more striking way the involvement of the scrotum adjacent to testicular foci lends itself to a similar interpretation. Although this phase of the study could not be entered into with the degree of completeness desired, a small series of experiments gave results sufficiently uniform to merit some discussion. Attempts to infect the opposite testicle in the course of active involvement, during the stages of marked regression, and after almost complete disappearance of palpable lesions in one testicle, resulted in the development of chancre-like lesions in the other, without giving rise at any time to the

characteristic process following intratesticular inoculation. A series of eight rabbits was injected in the normal testicle with material taken at different times from their respective infected testicles. Another series included animals that received homologous *Spirochaeta pallida* taken from other rabbits. The strain used was isolated from the inguinal gland of a case of latent syphilis. In the first group, 50 per cent. of the animals developed lesions in the subsequently inoculated testicle and in the second group, 75 per cent. The incubation period averaged from five to five and a half weeks. Dark-field examinations were characterized uniformly by a relative paucity of organisms. The scrotal lesions disappeared in from ten days to three weeks. Whether or not similar results may be obtained by the use of heterologous strains of spirochetes in an analogous manner is not known, since the object of the experiments was to determine roughly the infectivity of *Spirochaeta pallida* with a set of conditions tending to throw light on certain immune reactions. The outstanding feature of the experiments seems to be that the elaboration of syphilitic antibodies is not at its height early in the course of infection. This idea is borne out by studies on the protective properties of serum obtained from active and latent syphilis.

SURVIVAL OF SPIROCHAETA PALLIDA IN COMPLETELY HEALED TESTICLES OF RABBITS

Variations from the usual type of testicular infection in rabbits occur frequently. In some animals, at irregular times, slight changes may be found after inoculation with material from an actively infectious testicle, and again there are numerous instances of apparent failure to produce a "take." Influences which may modify the results of transfer from animal to animal have been discussed already, and attention will be given now to examples of "latent" *Spirochaeta pallida* in testicles which have proved continually negative by puncture for long periods, coincident with total disappearance of lesions, and in testicles which have remained negative for indefinite periods without having shown lesions or spirochetes at any time. In four instances we have succeeded in isolating *Spirochaeta pallida* from suspensions prepared with macerated testicles of rabbits which had been found negative by puncture and free from visible or palpable lesions for a period of from four to five months; twice in rabbits carrying a strain of spirochetes isolated from an inguinal gland of a patient with latent syphilis (Strain 137), once from a rabbit with a strain isolated from the semen of a latent syphilitic patient (Strain 117), and again from an animal which had been inoculated with spirochetes from a penile chancre.

SPIROCHAETA PALLIDA IN TESTICLES NEGATIVE BY PUNCTURE AND FREE FROM LESIONS

That certain conditions as they exist in the experimental animal may be paralleled in patients and deductions drawn accordingly would follow from the observations made in cases of latent syphilis¹ and in some of the present work. The tendency for *Spirochaeta pallida* to assume a dormant or latent state in the body is now an established fact. A brief consideration of the behavior of a single strain of organisms which has been studied intensively in our work may add more data from the immunologic standpoint. A group of rabbits representing the sixth generation of "latent strain 137" was characterized by progressively diminishing lesions and a pronounced tendency toward a negative picture in the testicle, irrespective of the character as to age and amount of material taken for subinoculation from the previous generations. Four animals which had been inoculated with spirochete-containing material from a rabbit in the sixth generation series failed to develop any lesions and were found negative by puncture for more than four months. A rabbit from this group was castrated and an emulsion of the inoculated testicle injected into the testicle of another rabbit which remained negative for a period of six weeks. This animal was castrated and the testicular emulsion injected into a third rabbit which developed a minute nodule after five weeks. The lesion, about 2 mm. in diameter, did not increase in size and was found to contain spirochetes over a period of two weeks when the lesion disappeared.

TABLE 7.—SUMMARY OF PROTOCOLS

Strain	Old Series	Survival of Spirochetes	Days Negative	Subinoculations
	Incubation Period Days			Incubation Period Days
137	28	22	116	34
137	35	66	138	48
117	28	31	116	42
169	30	29	120	41

CONCLUSIONS AND SUMMARY

The infectivity of *Spirochaeta pallida* derived from old lesions was not diminished by prolonged residence in an infected focus. No correlation seemed to exist between the period of incubation of the organism, on one hand, and the age of the lesion from which it was obtained, on the other.

Survival of *Spirochaeta pallida* in experimental syphilis was subject to marked variation. The persistence of spirochetes in rabbits' testicles was not correlated with the period of incubation, with the age

of the lesion, or with the number of animal passages of the different strains studied. Incomplete observations show that they may be present for more than five months.

Spirochetal content of lesions in the testicle was not correlated with the age of lesions and survival within the focus of infection. Fresh as well as old spirochetes did not appear to influence adaptation to environment as measured by survival, or to affect the period of incubation. No differences have been found to exist between different "lines of descent" made from a series of animals which represented transfers from actively developing lesions, and a series of generations which were derived from animals having old regressive lesions.

Although syphilitic manifestations in the rabbit testicle may exhibit a wide range of variability in their cyclic changes, certain outstanding features may be associated with definite strains of *Spirochaeta pallida*. A chronic proliferative type of reaction characterized organisms which had been isolated originally from cases of latent syphilis. The type of lesion, however, did not give an indication as to the fate of *Spirochaeta pallida* in such lesions. Scrotal lesions following as late manifestations of old testicular infection were not referable to particular strains.

Elaboration of syphilitic antibodies appeared to be at a maximum late in the course of infection and predisposed to a condition of latency in which, despite the absence of lesions, *Spirochaeta pallida* could be demonstrated. Far from preventing reinoculation with *Spirochaeta pallida*, a state of resistance appears to favor the localization of organisms in tissues without giving rise to manifest lesions.

Inoculated testicles which remained negative for indefinite periods, presenting no lesions, and proving negative by puncture, have been found to harbor *Spirochaeta pallida* capable of infecting other animals. The tendency for a condition of latency to occur was confined to certain strains of organisms, in particular those which had been isolated from latent sources in patients and rabbits.

In the absence of lesions and with negative dark-field findings over a period of four to five months, *Spirochaeta pallida* was isolated from apparently normal testicles which had previously been positive for spirochetes.

Sensitization phenomena may play an important part in the production of a certain kind of scrotal lesion resulting from autoinoculation of a normal testicle, from experimental infection of the opposite testicle in the course of involvement of the other, or from old testicular foci.

Seven strains of *Spirochaeta pallida* have been studied from the standpoints of infectivity and survival and differential characters. Five of the strains were isolated from cases of latent syphilis—inguinal glands and semen—and the others were obtained from penile chancres.

IS LUPUS ERYTHEMATOSUS DISCOIDES CHRONICUS DUE TO TUBERCULOSIS?

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The question of the relationship of lupus erythematosus to tuberculosis has interested dermatologists since the time of Cazenave, who gave the disease its present name, and considered it probably identical with lupus vulgaris. Very early most French observers, on the strength of their clinical observations, maintained that lupus erythematosus was of tuberculous origin, a paratuberculosis. Dermatologists of the English, Austrian and German schools, on the other hand, insisted that evidence favoring such a view was insufficient. Since that time opinions have varied. Recently certain American authorities¹ have expressed doubt as to the specific tuberculous origin of this dermatosis, and seem to favor multiple etiologic factors. Their conception, evidently based on a varied clinical experience, is in accord with my own. To verify my clinical impression I made this statistical study, approaching the question by four avenues:

1. The percentage of clinical tuberculosis detected in patients with lupus erythematosus discoides chronicus, who had been adequately studied for tuberculosis, was estimated.

2. The records were searched for patients with dermatoses ordinarily not associated with tuberculosis in order to determine, for comparative purposes, the frequency of clinical tuberculosis in these dermatoses. No record was used which did not show evidence of an adequate examination for tuberculosis.

3. The frequency of clinical tuberculosis in such dermatoses as erythema multiforme and erythema nodosum, probably in certain cases of tuberculous origin, was compared with the incidence of tuberculosis in lupus erythematosus discoides chronicus.

4. The incidence of tuberculosis shown by the records of patients with tuberculids, who had been adequately examined for tuberculosis, was compared with the frequency of tuberculosis in patients with lupus erythematosus discoides chronicus. It should be stated here that "patients adequately examined for tuberculosis" means patients who

1. Hartzell, M. B.: Lupus Erythematosus and Focal Infection, Arch. Dermat. & Syph. 2:441 (Oct.) 1920.

had been subjected to special examination for the detection of the disease in the medical sections and not merely to routine physical examination.

CLINICAL TUBERCULOSIS IN PATIENTS WITH LUPUS ERYTHEMATOSUS DISCOIDES CHRONICUS

Fifty-six patients in a group of 150 with lupus erythematosus discoides chronicus had been specially examined for tuberculosis. The records of the others were unsatisfactory for the purpose, either because the diagnosis of lupus erythematosus discoides chronicus had not been definitely made, or because the physical examination for tuberculosis was not adequate. Twenty (35.7 per cent.) of the fifty-six patients had tuberculosis, of whom eight (40 per cent.) had glandular involvement alone, and five (25 per cent.) had both glandular and other forms of tuberculosis. Seven of these patients (35 per cent.) showed signs of tuberculosis other than glandular. Four of these were reported as probably cured. It should be observed that 65 per cent. of the tuberculous lesions found in these patients were of the glandular type. Incidentally, it was noted in our group that the average age of the patient at the onset of lupus erythematosus discoides chronicus was 33 years. The youngest patient was 7 years when the disease began, and the oldest 59 years. These facts evidently do not constitute evidence for or against tuberculosis as an etiologic agent. Realizing the various difficulties that beset the examiner in obtaining a reliable family history of tuberculosis from the average layman, I do not wish to emphasize the significance of any data obtained from the histories alone; it may be stated, that our records gave a positive family history of tuberculosis in fifteen instances (27 per cent.) only. Four of these were in patients with definite tuberculosis infection at the time of examination.

FREQUENCY OF CLINICAL TUBERCULOSIS IN VARIOUS DERMATOSES

To find the frequency of clinically recognizable tuberculosis in dermatoses admittedly not of tuberculous origin, fifty-six records of patients with miscellaneous nontuberculous dermatoses, in whom an adequate examination for tuberculosis had been made, were taken at random from 252 successive histories searched to yield the required number. The only basis for selection was a special examination for tuberculosis. Included in the 252 cases were thirty-three cases of dermatitis herpetiformis, thirty-six of lichen planus, 145 of eczematoid dermatitis and thirty-eight of psoriasis. The total number of histories examined, the number of patients adequately examined for tuberculosis, and the proportion of positive findings of tuberculosis are given in the following table.

INCIDENCE OF TUBERCULOSIS IN MISCELLANEOUS DERMATOSES

Type of Dermatitis	Patients Adequately		Tuberculosis Present
	Patients	Examined	
Dermatitis herpetiformis.....	33	7	2 (28.5 per cent.)
Lichen planus.....	36	9	1 (11.1 per cent.)
Ecematoid dermatitis.....	145	29	11 (38 per cent.)
Psoriasis	38	11	4 (36.4 per cent.)
Total	252	56	18 (32.1 per cent.)

The table shows that the percentage of clinical tuberculosis in miscellaneous dermatoses is almost as high as the incidence of tuberculosis in lupus erythematosus discoides chronicus (32.1 per cent. compared with 35.7 per cent.). It should be noted, however, that there was only one case with glandular tuberculosis in this group.

FREQUENCY OF CLINICAL TUBERCULOSIS IN ERYTHEMA MULTIFORME AND ERYTHEMA NODOSUM

The incidence of tuberculosis in such dermatoses as erythema multiforme and erythema nodosum was next considered. This examination is of unusual interest because erythema multiforme and erythema nodosum are probably etiologically as closely allied to lupus erythematosus discoides chronicus as any dermatoses, in the sense that their cause is undetermined, but that much evidence points to a tuberculous factor in their etiology² in some instances, and their nontuberculous³ nature in others. The belief is gaining ground that other influences, for example, focal infections, may uncover the tuberculous lesion, so to speak, much as measles is known to uncover it and permit a lighting up of a lesion otherwise quiescent.⁴ Fifty-three patients with erythema multiforme and erythema nodosum in a group of ninety-six had been adequately examined for tuberculosis. Of these, seventeen (32 per cent.) had evidence of tuberculosis. Two facts are evident. The incidence of clinical tuberculosis in these dermatoses is slightly less (32 per cent.) than that in such admittedly nontuberculous dermatoses as those classified under the term eczemoid dermatitis (37.9 per cent.). Neither does the percentage exceed that in all the nontuberculous dermatoses considered (32.1 per cent.). It also compares favorably with the incidence of tuberculosis in lupus erythematosus discoides chronicus

2. Foerster, O. H.: The Association of Erythema Nodosum and Tuberculosis. *J. A. M. A.* **63**:1266-1268 (Oct. 10) 1914.

3. Rosenow, E. C.: The Etiology and Experimental Production of Erythema Nodosum. *J. Infect. Dis.* **16**:367-384, 1915.

4. Stokes, J. H.: Clinical Studies in Cutaneous Aspects of Tuberculosis. I. "Tuberculous" Purpura. Erythema Multiforme and Erythema Nodosum, *Am. J. M. Sc.* **157**:157-170, 1919.

(35.7 per cent.). These figures, while too small to be conclusive, suggest that erythema multiforme and erythema nodosum, like lupus erythematosus discoides chronicus may both at times be of tuberculous etiology, but that they may both at times be of nontuberculous etiology.

INCIDENCE OF CLINICAL TUBERCULOSIS IN THE TUBERCULIDS COMPARED
WITH ITS INCIDENCE IN LUPUS ERYTHEMATOSUS
DISCOIDES CHRONICUS

The most striking feature of this study was the contrast afforded by the incidence of clinical tuberculosis in the tuberculids when compared with its incidence in lupus erythematosus discoides chronicus. Thirty-seven cases of lichen scrofulosorum, erythema induratum, papulonecrotic tuberculids, folliculitis and acnitis (Barthélemy) had been adequately examined for tuberculosis. Of these, thirty-one (84 per cent.) presented definite clinical evidence of infection compared with 35.7 per cent. in lupus erythematosus discoides chronicus. The tuberculosis in eighteen (48.6 per cent.) was of the glandular type only, and in four (10.8 per cent.) both of glandular and of some other type. Six of the patients who presented negative findings had erythema induratum. The diagnosis of one of the six is still to be regarded as doubtful after prolonged observation. In none of the foregoing cases did we find an authentic instance of the simultaneous occurrence of lupus erythematosus discoides chronicus and tuberculids.⁵

The unimportant part played by tuberculosis in lupus erythematosus discoides chronicus, as compared with acknowledged tuberculids, is so striking that one is tempted to say flatly that lupus erythematosus discoides chronicus cannot have the pathogenesis of a tuberculid in the accepted sense of the term.

TUBERCULOSIS AS AN ETIOLOGIC AGENT

A review of the literature illustrates the difficulty of adding anything new to the evidence incriminating tuberculosis as an etiologic agent in lupus erythematosus discoides chronicus. It does not seem necessary to review here in detail the various arguments based on clinical observation. This has been done most thoroughly by Friedlander,⁶ Fresh-

5. Among the earlier records of the department I subsequently found one instance of such association, and such association has been reported by MacLeod, Wile and others. MacLeod, J. M. H.: A Case of Erythema Induratum. *Brit. J. Dermat.* **18**:406, 1906. Wile, U. J.: Widespread Lupus Erythematosus with Associated Papulo-Necrotic Tuberculide (?), *J. Cutan. Dis.* **29**:286-290, 1911.

6. Friedlander, D.: The Etiology of Lupus Erythematosus with Especial Reference to Tuberculosis and a Report of Thirteen Cases Tested by the Moro Reaction, *J. Cutan. Dis.* **29**:417-428, 1911.

water,⁷ Bloch and Fuchs,⁸ Wise⁹ and others. Most of the arguments are based on evidence aiming to prove the tuberculous nature of lupus erythematosus discoides chronicus by its frequent association with other evidence of tuberculosis. The double edged character of such arguments becomes apparent when such observers as Gunsett¹⁰ and Weiss and Singer¹¹ come to the conclusion that tuberculosis is not a factor in the production of lupus erythematosus discoides chronicus, on diametrically contrary observations. Gunsett collected from the literature twenty cases of lupus erythematosus in which careful post-mortem examinations had been made. In only nine of these was any evidence of tuberculosis found. Ten of the postmortem examinations were made under the direction of Rokitansky, and in seven instances no evidence of tuberculosis was discovered. Gunsett is well aware of the frequency of tuberculosis in general and justly lays special emphasis on the frequent impossibility of demonstrating on postmortem examination the presence of tuberculosis in lupus erythematosus discoides chronicus. In the light of our present knowledge it certainly seems that a carefully conducted postmortem examination is worth vastly more than all the combined clinical statistics endeavoring to show the coincidence of tuberculosis and lupus erythematosus discoides chronicus.

To Weiss and Singer the association of tuberculosis with lupus erythematosus discoides chronicus means chiefly the ubiquity of tuberculosis and is not evidence of any etiologic relationship. They found indubitable evidence of tuberculosis past or present in ten of their twelve patients, and they believe that the other two were also tuberculous. They emphasize the fact that investigators have found increasingly higher percentages of tuberculosis in their postmortem examinations, and they cite Opie¹² as being able to demonstrate tuberculous lesions in every one of fifty patients who died of nontuberculous diseases. This pathologist used a most ingenious method of postmortem investigation. Roentgen-ray pictures were taken of the inflated and extirpated lung followed by minute section and search with the skiagram as a guide. These observations suggest that tuberculosis is

7. Freshwater, D.: The Etiology of Lupus Erythematosus, *Brit. J. Dermat.* **24**:57-69, 99-115, 1912.

8. Bloch, B., and Fuchs, H.: Ueber die Beziehungen des chronischen Lupus erythematosus zur Tuberkulose, *Arch. f. Dermat. u. Syph.* **116**:742-803, 1913.

9. Wise, F.: The Relation Between Lupus Erythematosus and Tuberculosis, *New York M. J.* **107**:1164-1167, 1918.

10. Gunsett, A.: Ist der Lupus erythematosus ein Tuberkulid? *München. med. Wchnschr.* **50**:378-381, 1903.

11. Weiss, R. S., and Singer, J. J.: The Relation of Lupus Erythematosus Discoides to Tuberculous Infection, *Am. J. M. Sc.* **155**:528-540, 1918.

12. Opie, E. L.: Quoted by Weiss and Singer.

almost universal. Since lupus erythematosus discoides chronicus is a comparatively rare disease, these observations certainly suggest that factors of moment other than tuberculosis must enter into the etiology of the disease. The results of the present study support Weiss' and Singer's view not only because in nontuberculous dermatoses approximately as high an incidence of clinical tuberculosis as in lupus erythematosus discoides chronicus was apparent, but also because in lesions of the skin admittedly tuberculous, such as the tuberculids, the incidence of clinical tuberculosis is far higher. Weiss and Singer's tabulations of lupus erythematosus discoides chronicus cases correspond closely with my data. They found a total of 225 cases, in sixty-four of which the presence or absence of tuberculosis was noted. Of these sixty-four cases, eighteen (28 per cent.) showed evidence of tuberculosis and forty-six (72 per cent.) did not. Our combined observations seem to indicate that clinically recognizable tuberculosis is a factor in only a moderate percentage of cases of lupus erythematosus discoides chronicus. While clinical observation thus critically examined seems to give little encouragement to a belief in the tuberculous etiology of lupus erythematosus discoides chronicus, experimental investigation at times seems all but to have proved its tuberculous origin. When the results of these investigations are critically reviewed, however, the case for a purely tuberculous etiology does not seem nearly so strong.

Tuberculosis Demonstrated by Tuberculin Test.—It is, of course, not surprising that in cases of lupus erythematosus discoides chronicus, as in other diseases suspected of a tuberculous etiology, the tuberculin test should have been freely employed. It is at once apparent that only the focal reaction in the lupus erythematosus discoides chronicus lesion could possibly be of any significance. The von Pirquet, the intradermal and the general reactions are only of interest in so far as they signify tuberculous infection past or present. But as in a certain number of patients with lupus erythematosus discoides chronicus the systemic tuberculous infection is easily demonstrated clinically, and as tuberculosis is probably present in the majority of the remainder, as modern investigation tends to show, the tuberculin reaction is of little value. Fishberg¹³ found that between 40 and 60 per cent. of humanity react to the tuberculin test. Franz¹⁴ was able to obtain from 60 to 70 per cent. of positive tuberculin reactions in several Austrian regiments. It must be remembered that he was dealing with healthy men selected

13. Fishberg, M.: Quoted by Weiss and Singer.

14. Franz: Quoted by Deycke, p. 22.

because of exceptional physical fitness. Deycke¹⁵ states that in European countries it is only the exceptional adult who does not react to tuberculin. It would hardly seem that the systemic tuberculin reaction can be adduced as an argument to prove the tuberculous etiology of lupus erythematosus discoides chronicus.

The focal or local reaction in the lupus erythematosus discoides chronicus lesion has been looked on as favoring the tuberculous origin of lupus erythematosus, and such a phenomenon has been reported by some good observers. Engman and McGarry¹⁶ have repeatedly observed this reaction, however, on the injection of dead typhoid bacilli used as a foreign protein. Barber¹⁷ has observed a severe focal reaction following the injection of an autogenous vaccine prepared from a tonsillar swab which gave a pure growth of long-chain streptococci. Moreover, true cutaneous tuberculosis (lupus vulgaris) is known to give focal reactions to nonspecific agents, such as arsphenamin.¹⁸ It seems, therefore, that the focal phenomenon can be produced readily by other agents.

The fact that lupus erythematosus improves under the administration of tuberculin cannot be regarded as a valid argument for its tuberculous nature. Engman and McGarry, Barber, and Adamson,¹⁹ have seen patients definitely improve under the administration of other forms of internal medication. We have observed the disappearance of lupus erythematosus under a species of autogenous vaccination produced by an attack of erysipelas.²⁰

Demonstration of Tubercle Bacillus by Ziehl's and Much's Methods.—The demonstration of the tuberculosis bacillus directly by Ziehl's method in the sections from patches of lupus erythematosus has been frequently tried but never successfully accomplished. When the difficulty of demonstrating the bacillus by this method from the lesions of a known tuberculous nature, such as lupus vulgaris, is considered, it is not surprising that lupus erythematosus yields negative results. In recent years Much's method has enabled observers apparently to demonstrate

15. Deycke, G.: *Praktisches Lehrbuch der Tuberkulose*, Berlin, Springer, 1920, p. 23.

16. Engman, M. F., and McGarry, R. A.: The Treatment of Certain Diseases of the Skin by the Intravenous Injection of a Foreign Protein, *J. A. M. A.* **67**:1741-1745, 1916.

17. Barber, H. W.: A Case of Lupus Erythematosus Associated with Streptococcal Infection of the Tonsils, *Brit. J. Dermat.* **31**:186-193, 1919.

18. Herxheimer, K., and Altmann, K.: Ueber eine Reaktion tuberkulöser Prozesse nach Salvarsaninjektion, *Deutsch. med. Wchnschr.* **37**:441-443, 1911.

19. Adamson, H. G.: Discussion of Lupus Erythematosus, *Proc. Roy. Soc. Med., Sect. Dermat.* **13**:98, 1920.

20. Stokes, J. H.: Discussion of Lupus Erythematosus, *Arch. Dermat. & Syph.* **2**:445-446, 1920.

tuberculosis bacilli when it was impossible to find them by Ziehl's stain. The presence of Much's granules is not generally accepted, however, as proof of the tuberculous nature of any lesion. Their identity with tuberculosis bacilli is not universally accepted, and it is an acknowledged fact that it is often difficult to distinguish between Much's granules and artefacts in sections or smears.¹⁵ Positive demonstrations of tuberculosis bacilli are reported in only a few instances. The organisms were all found in excised pieces of tissue from lupus erythematosus treated by the antiformin method. Such cases have been reported by Arndt,²¹ Hidaka,²² Spiethoff,²³ and Friedlander.²⁴ These observers demonstrated the bacilli by both Ziehl's and Much's methods. Hidaka and Friedlander, however, are skeptical of their significance. The former does not consider Much's granules as proof of tuberculosis. He believes that tuberculosis bacilli may easily circulate in the blood of tuberculous persons, or that they may be simulated by acid-fast bacilli found in the water supply and accidentally introduced during the experiment. These positive findings need further confirmation before they can be accepted as having any significance. It should be said also that Arndt's cases were not of the chronic type. Granted that his observations were correct for the type of case he examined, it would not be proof that the chronic type did not involve some special factors of etiologic moment.

Tuberculosis Proved by Animal Inoculation.—Undoubtedly, the experiments of greatest significance are those in which positive animal inoculations have been obtained. A positive result is probably the most dependable proof obtainable, although errors may readily be committed here also. I was able to find in the literature records of only seven positive animal experiments, and these merit most careful scrutiny.

Gougerot²⁵ reported the first successful attempt at animal inoculation. His first patient had a typical lupus erythematosus of the scalp without other evidence of tuberculosis. The patch was excised and transplanted into two guinea-pigs. Five months after inoculation one animal did not reveal evidence of tuberculosis on section; the other had

21. Arndt, G.: Ueber den Nachweis von Tuberkelbacillen bei Lupus erythematosus acutus resp. subacutus, Berl. klin. Wchnschr. **47**:1360-1362, 1910.

22. Hidaka, S.: Ueber den Nachweis von Tuberkelbazillen und Muchschen Granula bei Lupus vulgaris, Lupus erythematosus, Erythema induratum Bazin, Lupus pernio und papulo-nekrotischem Tuberkulid, Arch. f. Dermat. u. Syph. **106**:259-276, 1911.

23. Spiethoff, B.: Zur Aetiologie und Pathologie des Lupus erythematosus chron. und Acut, Arch. f. Dermat. u. Syph. **113**:1047-1060, 1912.

24. Friedlander, D.: The Value of Much's Granules and the Antiformin Method in Determining the Etiology of the So-Called Tuberculides, with Especial Reference to Lupus Erythematosus, Brit. J. Dermat. **24**:13-20, 1912.

25. Gougerot, H.: Tuberculoses cutanées atypiques non folliculaires, Rev. de la tuberculose **5**:345, 1908.

two sclerotic matted glands with caseated centers at the site of the graft. In the caseous material a few tuberculosis bacilli were found. The liver and spleen also revealed a few small nodules with typical tuberculous structure. This case is probably the nearest approach to an experimental demonstration reported in the literature. It was evidently a typical case of lupus erythematosus discoides chronicus in a patient without other evidence of tuberculosis. The experimental evidence produced from cases with acute disseminate lupus erythematosus or from cases of an atypical type cannot be accepted as demonstrating a tuberculous etiology for lupus erythematosus discoides chronicus.

The second case reported by Gougerot is a freak or atypical lupus erythematosus. The case does not apparently belong even in the usually recognized subclasses of lupus erythematosus, but perhaps may be regarded as an example of a vesico-ulcerative type. When authorities hold widely divergent opinions relative to the etiology and nosology of such conditions as the various types of sarcoids, nodular tuberculosis of the hypoderm, granuloma annulare, erythema elevatum diutinum and allied dermatoses, certainly no atypical case of lupus erythematosus which may at times resemble any of these dermatoses should be used to prove the etiology of lupus erythematosus discoides chronicus. We must therefore conclude that Gougerot's second case cannot be accepted as an authentic lupus erythematosus discoides chronicus.

Ehrmann and Reines²⁶ reported a case of successful animal inoculation. In their patient the lupus erythematosus discoides chronicus was, however, associated with typical papulonecrotic tuberculids on the buttocks and large tuberculous glands of the neck. The significance of a positive animal inoculation from such a case remains open to discussion. The criticism of the experiment revolves largely around the presence of active tuberculous lesions in the body. In this particular instance the presence of a tuberculid speaks for hematogenous distribution of tuberculosis bacilli. The hematogenous distribution of tuberculosis bacilli may at least be regarded as fairly well supported, for example, by the observations of Liebermeister,²⁷ who believed himself able to demonstrate the tuberculosis bacilli in the blood of living patients. He not only found them in advanced stages or when the patient was moribund, but also in a number of clinically mild cases. On the basis of his experimental and pathologic observations, he concludes that tuberculosis bacilli are in every case periodically projected

26. Ehrman, S., and Reines, S.: Zur Frage des Lupus erythematoses und der Tuberkulide überhaupt. *Med. Klin.* **4**:1298-1302, 1908.

27. Liebermeister, G.: Studien über Komplikationen der Lungentuberculose und über die Verbreitung der Tuberkelbazillen in den Organen und im Blut der Phthisiker. *Virchows Arch. f. path. Anat.* **197**:332-425, 1909.

into the blood and that they may circulate in the blood without producing a miliary tuberculosis or typical metastasis. It is an accepted fact that tuberculosis of the kidney, in the vast majority of instances, is of hematogenous origin. O'Neil²⁸ says, "There is ample evidence to show that the bacilli are carried to the kidney by the arterial blood in a great majority of cases. Blood infections in tuberculous patients are not uncommon, and it is a well established fact that even with a small tuberculous focus in an active state, such as an apical lesion, there may be a temporary bacillemia during which time the bacilli may be recovered from the blood. Further evidence that tubercle bacilli reach the kidney more or less constantly is shown by numerous observations that in pulmonary tuberculosis a filtration of bacteria may take place through the kidneys which after death show no evidence of tuberculous disease." Presence of tuberculosis bacilli in the circulating blood should warn us not to lay too much stress on the presence of these bacilli in excised pieces of tissue. The demonstrated bacilli could in certain instances have been present in the capillaries of the lesion. This presence of bacilli in the capillaries could easily occur in early lesions of lupus erythematosus discoides chronicus with their marked vascular dilatation and blood stasis.

Probably no experimental work on the tuberculous nature of lupus erythematosus discoides chronicus has been more carefully controlled than that of Bloch and Fuchs.⁸ These authors review carefully all the evidence brought forward for or against the tuberculous etiology of the condition. They conclude that unless it is the results of positive animal inoculation, none of the evidence brought forward in behalf of tuberculous etiology is so strong that other evidence equally valid cannot be found to offset it. Believing that positive animal inoculations would be the only conclusive proof, these observers made determined efforts to produce tuberculosis in guinea-pigs by inoculating them with pieces of the tissue from lupus erythematosus. They were able to demonstrate tuberculosis bacilli in four cases. In two instances in the first series of animals the inoculation was successful, once in the second series, and once not until the third series. The authors believe that their success was due to repeated animal passage; the gradually increasing virulency of the bacillus finally produced tuberculous lesions in the experimental animal. Here again the value of the experiments is impaired by the fact that three of the patients had active tuberculosis. One of the patients had an active disseminate lupus erythematosus which closely resembled the type first described by Kaposi as *erysipelas faciei perstans*. This case must be eliminated because of the doubtful nosologic classi-

28. O'Neil, R. F.: Tuberculosis of the Kidney and Ureter, in Cabot, H.: *Modern Urology*, Philadelphia, Lea & Febiger 2:496, 1918.

fication of the dermatosis. The fourth case, while not clinically tuberculous, reacted severely to 1 mg. original tuberculin. In all of these cases the possibility that the patient's blood contained circulating tuberculosis bacilli and that, as Liebermeister suggests, these might have lodged in the capillaries, must be considered. Certainly it would seem that much better material to prove the purely tuberculous etiology of lupus erythematosus discoides chronicus could have been chosen. To prove that lupus erythematosus discoides chronicus is a true tuberculosis, typical cases of lupus erythematosus discoides chronicus without other clinical manifestations of tuberculosis should be selected. There is an abundance of such material, as the cases reported in the English and American literature and those in this series readily attest. It may be that such experiments have been made and proved uniformly negative, and therefore have not been reported. To date the only case of positive animal inoculation that will endure a critical review is the first case reported by Gougerot. Even here accidental retention of bacilli in the morbid process is not eliminated. This case, however, is only a single instance and needs confirmation before it can be accepted at its face value.

Cutaneous Allergic Phenomena.—In a consideration of reactions of the skin many suggestive points bearing on a possible nonspecific character in the tuberculin reaction in lupus erythematosus discoides chronicus may be found. The allergic reaction of the skin to substances introduced intradermally is now well recognized in a number of clinical conditions. The conception of a nonspecific element in this phenomenon has received important support from the study of cutaneous allergic phenomena in late syphilis. Such apparently specific substances as Klausner's palladin and Noguchi's luetin have been shown to produce their reaction by a nonspecific mechanism. Boas and Stürup²⁹ demonstrated a typical palladin reaction in late syphilis by using extracts of chancroidal bubo from a nonsyphilitic patient. Boas and Ditlevsen³⁰ duplicated this experiment by producing a luetin reaction in late syphilis with gonococcal and colon bacillus suspension. Sherrick³¹ has gone a step farther and evidently artificially produced by the administration of iodids the cutaneous allergic state. He also observed that such colloidal substances as agar and starch gave similar reactions. Probably his most interesting observation was his reactiva-

29. Boas, H., and Stürup, J.: Untersuchungen über Kutanreaktionen mit Organextrakten bei Syphilitikern, *Arch. f. Dermat. u. Syph.* **120**:730-738, 1914.

30. Boas, H., and Ditlevsen, C.: Untersuchungen über Noguchis Luetinreaktion, *Arch. f. Dermat. u. Syph.* **116**:852-864, 1913.

31. Sherrick, J. W.: The Effect of Potassium Iodid on the Luetin Reaction, Preliminary Report, *J. A. M. A.* **65**:404-405 (July 31) 1915.

tion of a practically involuted luetin reaction by subsequent administration of iodids. Stokes³² showed that agar makes an entirely satisfactory substitute for luetin in the luetin test applied in late syphilis, and that the reaction and the allergy on which it depends are alike nonspecific. He was also able to produce, artificially, a cutaneous allergy clinically similar to that produced in late syphilis by the injection of an homologous protein in the form of an emulsion of normal skin. By a series of injections he produced a reactivity to agar which in all respects experimentally imitated the allergy of late syphilis. These observations are essentially a proof that cutaneous allergy of certain types as observed in a disease like syphilis can be imitated artificially by the introduction of proteins other than those of the specific organisms of the disease. Thus far tuberculin reactions seem usually to have been regarded as specific antigen-antibody phenomena. The similarity of allergic phenomena in the skin in tuberculosis and in late syphilis makes the conception that the tuberculin reaction may be less specific in character than is generally supposed seem not unreasonable. Jadassohn's³³ attempt to explain his observations on tuberculin reactions in certain syphilitic lesions by what he calls "group reactions" are not without interest in this connection. Ingenious theories have been devised to explain the failure to react to tuberculin in certain types of tuberculous subjects. The possible lack of specificity in the reagent and the absence of certain specific factors usually seem to be overlooked. It must be conceded, however, that experimental proof of the completely nonspecific character of the tuberculin reaction is apparently lacking unless that produced by Meirowsky³⁴ can be accepted as such.

Whether or not we accept the allergic phenomenon as specific in character, the interesting intradermal injection experiments conducted by Bloch and Fuchs and used to support the theory that lupus erythematosus discoides chronicus is tuberculous in etiology are open to other interpretations than those the authors adopt. They injected intradermally extracts made from lupus erythematosus tissue into patients hypersensitive to tuberculin and argued from the reactivation of the papule by the subsequent injection of tuberculin that the extract contained either the bacilli or their toxins. Stokes conducted an experiment

32. Stokes, J. H.: Studies on Intradermal Sensitization. I. Intradermal Reactions to Emulsions of Normal and Pathologic Skin, *J. Infect. Dis.* **18**: 402-414, 1916. II. An Intradermal Reaction to Agar and an Interpretation of Intradermal Reactions, *ibid.*, p. 415.

33. Jadassohn, J.: Einige Erfahrungen über lokale Reaktionen mit Moroscher Tuberkulin-Salbe bei Hauttuberkulose, Tuberkuliden, Syphiliden und Lupus erythematosus, *Arch. f. Dermat. u. Syph.* **113**:479-504, 1912.

34. Meirowsky, E.: Ueber die diagnostische und spezifische Bedeutung der v. Pirquetschen Hautreaktion, *Arch. f. Dermat. u. Syph.* **94**:335-364, 1909.

in which the experimental conditions were similar to those of Bloch and Fuchs to prove the nonspecific character of intradermal reactions. His patient was a late syphilitic with psoriatic lesions. Emulsion of the normal skin given intradermally gave a definite nodular reaction. Another injection of emulsion of a psoriatic lesion not obtained from the patient's skin, given seven days later, not only formed a definite nodule but produced a striking increase in the size of the first nodule. From the observation of this author it may be argued that in a sensitive person cutaneous allergic phenomena may be obtained with a nonspecific substance, such as emulsion of the skin of a healthy person. Thus nonspecific allergic responses may be obtained perhaps from an emulsion of tissue made from a lupus erythematosus lesion when injected into a subject highly sensitive to tuberculin. Bloch and Fuchs' inference that the lupus erythematosus lesion contains either dead tuberculous bacilli or their toxins can scarcely be unqualifiedly accepted. Another weakness of the intradermal tests performed by Bloch and Fuchs is that they used not only emulsions of lupus erythematosus, but that by doing this they actually used skin from admittedly tuberculous patients. To make their tests more significant a control should have been instituted by using for the control emulsion apparently healthy skin from the patients to learn whether the same phenomena might not have been produced as was produced by the emulsion from the lupus erythematosus lesion.

COMMENT

It is apparent, therefore, that the tuberculous origin of lupus erythematosus discoides chronicus has not been proved by any of the experimental methods reported. The most modern and comprehensive clinical studies, on the other hand, definitely favor a belief in varied etiologic factors. It seems experimental work endeavoring to prove this latter conception is more promising than attempts to prove its purely tuberculous etiology.

CONCLUSIONS

1. The incidence of clinical tuberculosis in dermatoses admittedly of nontuberculous origin (32.1 per cent) is approximately as high as in lupus erythematosus discoides chronicus (35.7 per cent.).

2. Clinical tuberculosis is no more frequent in dermatoses-like erythema multiforme and erythema nodosum (32 per cent.), in some instances apparently of tuberculous origin, than in lupus erythematosus discoides chronicus (35.7 per cent.).

3. The frequency of clinical tuberculosis in patients with known tuberculids (84 per cent.) presents a striking contrast compared with the frequency of clinical tuberculosis observed in lupus erythematosus

discoides chronicus (35.7 per cent.). This contrast is so great that the belief seems acceptable that lupus erythematosus discoides chronicus cannot have a pathogenesis identical with that of the tuberculids.

4. The tuberculous origin of lupus erythematosus discoides chronicus has not been proved by experimental work. Clinical observation, including this statistical study, seems to favor varied etiologic factors.

A CONTRIBUTION TO THE CHEMOTHERAPY OF RHUS DERMATITIS AND TENTATIVE METHOD FOR TREATMENT

JAMES B. McNAIR

WASHINGTON, D. C.

The object of chemotherapy in rhus dermatitis (caused by *Rhus diversiloba*) is to imitate nature's method of overcoming the poison (lobinol) by the aid of substances that destroy the poison while the body cells are left unharmed or only slightly injured. The chemical agent employed, therefore, must possess a much stronger affinity for the toxic substance than for the body cells, that is, it must be more toxitropic than organotropic.

NECESSARY QUALIFICATIONS FOR THE REMEDY

In order best to accomplish this, the remedy should render the poison harmless, relieve pain, prevent sepsis, and aid in restoring the tissues injured by the poison to a normal condition. It may, therefore, be necessary to use two different formulas to be applied successively: one formula to neutralize the poison physiologically, and another formula to relieve pain, prevent bacterial infection, reduce the subsequent inflammatory changes in the cutaneous tissues and promote healing.

In order to choose the most fitting substance physiologically to neutralize this poison it is necessary to consider, apart from its chemical action on the poison, many other factors, such as its capacity for irritating the tissues, its toxicity, its solubility, its power of penetrating the tissues and of being absorbed by them, and the manner in which it reacts with the protein and other constituents of the tissues.

CHEMICAL NATURE OF THE POISON

It has been determined (McNair,¹ 1921) that the principal irritant of *Rhus diversiloba*, if pure and not a mixture, is probably an unsaturated compound of the aromatic series containing carbon, hydrogen and oxygen. The oxygen may exist combined as hydroxyl. The behavior of the poison is phenolic, and it may contain two hydroxyl groups in the ortho position.

1. McNair, J. B.: Lobinol—A Dermatitant from *Rhus Diversiloba* (Poison Oak), J. Am. Chem. Soc., January, 1921.

PROPHYLACTIC SUBSTANCES

The first problem in prophylactic treatment is to prevent the penetration of the poison into the skin. This can be considered in regard to the aid of solvents and precipitants.

Lobinol (McNair,¹ 1921) is soluble in ether, chloroform, alcohol, methyl alcohol, benzin, (boiling point below 60 C.) benzene, toluene, xylene, ethyl acetate, nitrobenzene, oil of turpentine, glacial acetic acid, and 80 per cent. chloral hydrate. The above solvents could be used as washes to remove the poison from the surface of the skin, provided they were not injurious. All of the solvents, however, are deleterious and some of them have a decidedly harmful action on the skin, such as glacial acetic acid, turpentine, benzene, nitrobenzene, and chloral hydrate.

Von Adelung² (1913) carried out the following experiments with solvents. Equal parts of 10 per cent. tincture of rhus and cotton seed oil, castor oil, and cedar oil were rubbed on separate areas of the arm. In thirty-six hours the cedar oil mixture caused a slight eruption, which later developed into a fair patch of itching dermatitis. After the castor oil mixture had been applied for thirty-six hours there was a slight itching, but no eruption. The mixture containing cotton seed oil produced no dermatitis. In considering these results, von Adelung considered the possibility of cotton seed oil chemically combining with the poison and destroying its toxicity. However, when the mixture of oil and tincture were allowed to stand several days, the tincture formed a supernatant toxic layer. It is probable that the different degrees of dermatitis produced by these mixtures varied in accordance with the solubility of the poison in the oils involved. For instance, when phenol is made up in solutions with water, alcohol, glycerin, turpentine and cotton seed oil, it has been determined that when fingers are immersed in them the blanching, tingling sensations and anesthesia are greatest in the water solution and decrease as follows: alcohol, glycerin, turpentine and cotton seed oil. The solubility of phenol in these instances varies in the reverse order of its anesthetic effect. Therefore, if the results of von Adelung with the tincture of rhus are comparable, the solubility of lobinol is greatest in cotton seed oil, less in castor oil, and least in cedar oil.

From a practical standpoint, the removal of the poison from the skin by the use of solvents seems quite futile, for, unless a sufficiently large amount of solvent is used to remove the poison thoroughly the poison will be spread on the surface of the skin and thus enlarge the

2. Von Adelung, E.: An Experimental Study of Poison Oak, *Arch. Int. Med.* **11**:148-164, 1913.

diseased area. Then, too, lobinol has the power to form either a physical or chemical compound with the skin of such a nature that it is quite impossible to remove with soap and water or with solvent action.

Lobinol is precipitated from alcoholic solutions by lead acetate, silver nitrate, mercurous nitrate, cupric acetate, ferric chlorid, barium hydroxid, bromin, iodine, platinum chlorid, gold chlorid, uranium acetate and cupric nitrate. Some of these precipitants, for example, tincture of iodine, must be used in dilute solutions, in order to prevent harmful action on the skin. Some of the precipitates formed by these substances are still toxic, such as the precipitate formed with lead acetate.

It is theoretically possible to remove the poison, before it has penetrated or firmly adhered to the skin, by the combined action of both solvent and precipitant, for instance, by the use of an alcoholic solution of lead acetate.

CURATIVE SUBSTANCES

If the poison succeeds in penetrating the skin, it should be rendered harmless as quickly as possible. The chemotherapeutic agent, therefore, must have a penetrability and diffusibility greater than the poison.

If lobinol contains a polyhydrophenol group, it has consequently several possibilities of being changed to a nonpoisonous substance or substances. Among these processes is oxidation. Some of the oxidizers that have been used are potassium permanganate, potassium bichromate, silver nitrate, hydrogen peroxid, manganese peroxid, barium peroxid, magnesium peroxid, litharge, and manganese hydroxid. If these substances be added in laboratory glassware to the poisonous sap of the plant, it will be observed that potassium permanganate, silver nitrate, manganese peroxid, barium peroxid, magnesium peroxid litharge, and manganese hydroxid have the power, after a more or less lengthy period of contact, to render the poison harmless. Some of these substances, for instance, litharge and barium peroxid, because of their insolubility and inability to penetrate the skin, cannot be used as remedies. Silver nitrate becomes too irritating when used in sufficiently strong solution. Many substances which enter into the composition of the tissues inhibit its action in a marked manner. The sensitivity to light and the staining property of silver compounds are also objections to their use. Von Adelung² (1913) has shown that hydrogen peroxid was without appreciable beneficial effect, while potassium permanganate did have the power to render the poison nontoxic. Potassium permanganate, however, has an injurious action on the skin and is not as efficient a remedy as some other remedies, as will be shown later.

Lobinol has an ability to react with nitric acid, probably due to its phenolic properties, to form a nitrated compound. As is well known,

nitric acid, even in dilute solution, stains the skin a bright yellow or yellowish-brown, which makes its use undesirable.

Lobinol evidently has the property of forming compounds with sodium and potassium, but both of these when first formed are poisonous.

Bromin and iodine form compounds with the poison, probably owing to its unsaturated nature. When experimented with in vitro, these halogens reduce the toxicity. When applied to the skin, however, they coagulate the proteins and irritate the tissues. The following five iodine compounds were experimented with: ethyliodid, iodol in alcohol, iothion, iodipin, (iodized sesame oil) and colorless tincture of iodine. In trying these substances, five areas of skin, of practically the same thickness, on the flexor surface of the forearm, were inoculated with equal amounts of fresh *Rhus* sap. These different areas were protected by doughnut shaped corn plasters, and the various iodine preparations were applied. The benefit derived from these substances increased in the following order: colorless iodine, iodipin, iothion, iodol in alcohol and ethyl iodid. None of these, however, were very beneficial, either in reducing the pain or in promoting healing.

The best success in the search for a remedy was obtained by taking into consideration the body defense against phenolic compounds. Whether or not lobinol has the power to form an ester with glycuronic acid, either within the body or in laboratory glassware, has not been determined. With an idea that glycuronic acid might be formed from glucose by the action of the body cells, a 5 per cent. aqueous solution of chemically pure crystalline glucose was applied to an area of rhus dermatitis. Although glucose has a slight irritant action on the skin, as is exemplified in diabetes mellitus, healing was promoted more rapidly in the area to which the glucose had been applied than in a check patch of dermatitis on which no remedy was used.

The power of lobinol to form a sulphonic ester in the body is quite probable. With this in view the following nine sulphur compounds were used similarly to the iodine preparations: sodium sulphate, sodium ethyl sulphate, sodium pyrosulphate, sodium dithionate, sodium sulphite, sodium ethanol 1,2-diacidsulphite, sodium pyrosulphite, sodium thiosulphate and taurin. Of these nine preparations, sodium sulphite and sodium ethanol 1,2-diacidsulphite gave the best results. These results, too, were superior to any results previously listed in this paper.

It is likely that iron may be one of the chemical elements enrolled in the body defense mechanism. As a tissue source of this there are the erythrocytes and protein. Whether or not the iron of the body plays a part in the physiologic neutralization of lobinol, cannot at present be stated. Ferric chlorid, however, despite its coagulating effect on

protein and irritant properties, with the possible exception of sodium sulphite and sodium ethanol 1,2-diacidsulphite has been found to be the most efficient remedy for the disease. At my suggestion a 5 per cent. mixture of ferric chlorid in 50 per cent. aqueous glycerol has been successfully used on bed patients with severe cases at the infirmary of the University of California. Its use there was discontinued on account of the iron staining the bed linen.

If further opportunity presents itself for continued experimentation on the chemotherapy of this disease it is hoped that a preparation may be found which, like those of Ehrlich in syphilis, will be more toxitropic, less organotropic, and have fewer of the disagreeable features of the substances presented herewith.

CLASSIFICATION OF THE CHEMOTHERAPEUTIC AGENTS ACCORD-
ING TO THEIR ACTION IN VIVO AND IN VITRO

The chemotherapeutic agents in rhus dermatitis may be classified according to the manner in which they react with lobinol.

1. A substance may render the poison nontoxic when in vitro, but not necessarily exert this effect in vivo. Litharge, for example, although it is able to decrease the toxicity of lobinol when in laboratory glassware, is unable to cure rhus dermatitis because of its insolubility and consequent inability to penetrate the skin.

2. Some substances capable of therapeutic effect under certain conditions are without effect in others, either in vivo or in vitro. For instance, solvents are ineffective in removing lobinol after it has firmly combined with the skin. Some remedies when too highly diluted also fail.

3. Substances exerting a marked effect in vivo may have no effect in vitro.

Solutions of dextrose, sodium sulphite, or magnesium sulphate in sufficient dilution are without apparent reaction on lobinol in vitro, yet when applied to rhus dermatitis in its initial stages they have a marked therapeutic value. This effect may be brought about by the remedial substance undergoing some modification in the body cells, so that it is changed into an active agent and unites with lobinol to form a corresponding physiologic neutral ester or other comparatively harmless substance. Like phenolic compounds, lobinol may probably form an ester with either glycuronic acid or sulphuric acid. Glycuronic acid probably has its origin in the body from dextrose through the oxidation of its terminal alcohol group. Such oxidation, however, could only take place when the aldehyde group is protected from oxidation.

Magnesium sulphate, which has been found of benefit in this disease by von Adelung (1913), may owe its effect not so much to its chemical action on the poison as to its salutary effect on the nerves. A review of the experiments of Solis-Cohen³ with magnesium sulphate on the nervous system points in this direction. Meltzer⁴ (1918) has shown the beneficial effect of a 25 per cent. solution in experimental first and second degree burns.

An effect in vivo and not in vitro may also be obtained by interference with the toxic function of lobinol without its direct chemical change, for example, substances which harden the skin or increase the thickness of the corium.

Part of the remedial value of iodine, picric acid, and ferric chloride in rhus dermatitis may be due to their ability to form a layer of precipitated and denatured protein on the injured surface. This layer acts as a protection not only against the penetration of the poison, but also against air and traumatic injury. An effect in vivo and not in vitro may possibly occur also merely by a stimulation of the natural protective mechanisms with or without the assistance of either of the foregoing methods.

4. Substances may have a destructive action on the toxicity of lobinol both in vitro and in vivo, for example, ferric chloride, iodine and potassium permanganate.

TENTATIVE METHOD FOR EXTERNAL TREATMENT

Rhus dermatitis, like burns, may be classified into three degrees of intensity as follows:

First Degree—Hyperemia or Erythema.—The skin has a bright red or purple hue, which disappears temporarily under the pressure of the finger and which gradually blends with the normal color of the skin around. There is a transitory swelling of the poisoned area, with perhaps slight oozing of serum from the surface. The superficial layers of the cuticle usually peel off later.

Second Degree—Vesication.—This stage has all the features of the first degree in aggravated extent. Some hours later vesicles appear. No permanent scar remains after the healing of this degree of dermatitis, but the part may show for a time a slight depression or dark colored pigmentation. Infection by septic bacteria may induce superficial suppuration and so delay repair.

3. Solis-Cohen, S.: The Analgesic Effect of Local Applications of Solutions of Magnesium Sulphate and Other Salts, J. A. M. A. **53**:1892 (Dec. 4) 1909.

4. Meltzer, S. J.: The Application of a Concentrated Solution of Magnesium Sulphate to Scalds and Burns, J. Pharmacol & Exper. Therap. **12**: 211-214, 1918.

Third Degree—Destruction of True Skin.—This seldom occurs in rhus dermatitis. When it does, permanent scars form.

Until further opportunity for experimentation and clinical observation occurs, Barthe de Sandfort's⁵ (1914) paraffin treatment of burns is given as tentative for the more severe cases of rhus dermatitis.⁶

5. De Sandfort, Barthe: De la kérithérapie (nouvelle application thermique des paraffines), 3rd Série **71**:560-562.

6. In addition to the references already given, the following may be of interest:

Anonymous: The Leukocyte Count as a Guide to Treatment of Wounds, Brit. M. J. **1**:465-466, 1917.

Sollmann, T.: Convenient Devices for Melting Paraffin for Burns, J. A. M. A. **68**:1895-1896 (June 23) 1917.

Correspondence

DERMATOLOGIC ETYMOLOGY

To the Editor.—I was much interested in the article which appeared in the April number on "Dermatologic Etymology" by Dr. George Henry Fox, and I hope that it will be published in pamphlet form so that it may be easily accessible. Most of the present-day textbooks on dermatology omit this information, which perhaps does not properly belong in them. Many of the medical dictionaries do not contain it, and the oversupply and depreciated price of secondhand Greek dictionaries indicate that the medical student does not search for it in such books. Some knowledge of the meaning of the names used in dermatology is of great assistance to the beginner, and Dr. Fox has furnished it in an interesting form and so compactly that it would be a pity not to have it separately obtainable.

I was amused at the slightly apologetic ending of the article. First because the name of Fox has so long held such a position in the dermatologic world that any apology for any dermatologic writings by any Fox is unnecessary. Second, because I surmise that he was apologizing to himself for writing on the *genealogy* of dermatologic terminology instead of confining himself to *dermatology*.

I may be mistaken in this, but in any case, had he desired to do so, he might have cited an excellent dermatologic precedent for his article in Robert Willan. Willan, though not a genealogist, was a fellow of the Society of Antiquaries and read before that Society, and later published, "A List of the Antient Words at Present Used in the Mountaneous District of the West Riding of Yorkshire."¹ In this list are a number of old popular medical terms, but there is no need of referring to them.

It is surprising that Dr. Fox was able to restrain himself from wandering beyond the limits he had planned for his article, when so excellent an opportunity for a genealogic (sic) excursus was presented by the word *syphilis*, the origin of which has been the subject of considerable speculation. Fracastor, who first used it in his poem, admitted the paternity, sixteen years after the birth of the child, in his book, "De Contagionibus et Contagiosis Morbis," saying "It was I who, in my poetical writings, first gave it the name of Syphilis."² But he never revealed the maternity of his child, and after his death Fallopius began to investigate the question and came to the conclusion that the mother was the Greek *σύν-φιλέω*, the companion of love. Dr. Fox accepts Fallopius' account of the maternity, and I, not being a genealogist, would not think of disputing it. Some derive it from another Greek origin, some from Hebrew, some from Arabic, and Pflug, the latest writer on the subject I have run across, derives it from the Sanskrit.

1. *Archaeologia* **17**:138-167, 1811; reprinted in *English Dialect Society*; reprinted *Glossaries*, London **2**:76-98, 1873.

2. Fournier's edition of Fracastor, Paris, 1869, p. 154.

I had at one time thought of summarizing the different views in a brief article, but gave up the idea as I knew I could only make it as dry as dust. Dr. Fox, dermatologist, syphilographer, genealogist and etymologist, can do it and make it interesting, and in order to stimulate and assist him, I append a few references on this subject:

Buret, F.: Syphilis in Ancient and Prehistoric Times. Translated by Ohmann-Dumesnil, Philadelphia, F. A. Davis Co., 1891.

Downing, A. F.: Syphilis: The Story of Its Treatment, Old and New, Boston M. & S. J. **177**: 715-720, 1912.

Pflug, W.: Syphilis oder Morbus Gallicus? Eine etymologische Betrachtung, Trübner, Strassburg, 1907.

Turner, E.: L'etymologie du mot syphilis; les premiers livres publiés sur cette maladie jusqu'à l'apparition du poème de Fracastor, Ann. de dermat. et syph. **3**: 423, 489, 564 and 665, 1882.

Späth: Einige Worte über die Etymologie des Worts Syphilis, Med. Cor.-Bl. d. Würtemb. aerzt. Ver. Stuttg. **11**: 49, 1841.

Timmermans, A.: De l'Etymologie du mot syphilis, J. d. mal. cutan et syph. **10**: 410-420, 1898.

I am sure that Dr. Fox will not be able to resist the title, "Eine etymologische Betrachtung," which Pflug gave his monograph.

JOHN E. LANE, M.D., New Haven, Conn.

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News and Comment

MEETING OF MINNESOTA DERMATOLOGICAL SOCIETY

The Minnesota Dermatological Society will hold its meeting on Aug. 5 and 6, 1921. The society will meet on August 5 at the Medical School of the University of Minnesota, Minneapolis, and on August 6 at the Mayo Clinic, Rochester, Minn. Both sessions will be clinical in character. At the conclusion of the first day's session at Minneapolis, the trip to Rochester will be made by automobile or train, arriving at Rochester on the evening of August 5. Visiting dermatologists will be welcome to attend the meetings.

Abstracts from Current Literature

LE MARIAGE DES SYPHILITIQUES (THE MARRIAGE OF SYPHILITICS). Committee Report, Bull. Soc. franç. de dermat. et syph. **8**:319, 1920.

This is the discussion of a committee report which was published in a recent issue of this bulletin (page 232, 1920). The following typical phases of the matter were considered:

1. The patient is seen and treated in the primary period and before the appearance of secondary symptoms or of a serologic reaction. Such a patient, responding favorably to a year's intensive treatment, would be permitted to marry at the end of the second year, during which time constant observation must show freedom from syphilitic manifestations, both clinical and serologic.

The treatment must be intensive and the laboratory must be dependable. Darier urges moderate treatment during the second year, and Leredde emphasizes the necessity of considering the individual quality of the syphilis in each case. Goubeau would extend the period to three years, and he would also give some treatment after marriage. Balzer would extend the time to four or five years, with more treatment, and Thibierge says two years should be the minimum.

2. The patient is seen and treated after the appearance of serologic reactions or even after the appearance of secondary symptoms. Here the committee favors two years' intensive treatment followed by a two years' surveillance with occasional tests of the blood and spinal fluid.

Goubeau would advise treatment extending over three years, with permission to marry at the end of that time providing the patient has early become and remained clinically and serologically negative. In any case, he says, the time should be x plus three years, x representing the length of time required to abolish all symptoms. Jeanselme counsels against pronouncing a cure too soon on purely laboratory grounds, for a negative reaction, even after a long time, may be replaced by a positive reaction. Thibierge follows the plan of Fournier, with four years of treatment and a period of eighteen months after the last manifestation.

3. If there is an irreducible blood serum reaction with a normal spinal fluid, five or six years of treatment are advised, and if the patient is a woman she should receive treatment thereafter when pregnant.

4. If in spite of the treatment indicated, the seroreaction being positive or negative, the spinal fluid shows a meningeal reaction and if prolonged treatment fails to dispel the symptom, marriage is contraindicated.

5. If the patient presents symptoms of involvement of the nervous system, marriage is interdicted. However, Leredde cautions against interpreting as syphilitic every irregularity of the pupil, or every alteration in the knee reflex.

6. If the candidate is an old syphilitic patient who can furnish only vague data concerning his previous treatments and if there are nervous symptoms, marriage is forbidden. If the blood or the spinal fluid shows a positive reaction thorough treatment is indicated. In a case entirely negative, and negative also after a provocative test, a year's treatment should be sufficient.

A syphilitic woman must be more thoroughly scrutinized than a man before being allowed to marry, and whenever pregnant she should be treated.

The question of "mariage blanc" is briefly discussed, and also that of the marriage of congenital syphilitics. The plan for the treatment of congenital syphilis is much the same as that for acquired syphilis, and irremediable organic lesions are a permanent contraindication to marriage.

PARKHURST, New York.

THE VALUE OF THE WASSERMANN REACTION IN OBSTETRICS.
BASED ON THE STUDY OF 4,547 CONSECUTIVE CASES.

J. WHITRIDGE WILLIAMS, Johns Hopkins Hosp. Bull. **31**:335 (Oct.) 1920.

A study was made of 4,547 pregnancies in which a Wassermann test was made, in each case, on the maternal and fetal blood. The placenta was examined microscopically, and if the child died within the first two weeks of the puerperium, necropsy was performed if possible. These conclusions were reached.

1. It is hazardous to draw any conclusion concerning the condition of the placenta or of the child from the existence of a positive maternal Wassermann reaction during pregnancy.

2. The existence of a positive Wassermann reaction on the part of the mother does not necessarily mean that her child will develop syphilis.

3. A positive Wassermann reaction at birth does not necessarily imply that the reaction will remain positive; and conversely, a negative Wassermann reaction at birth does not necessarily mean that it may not become positive later.

4. Demonstration of syphilitic changes in the placenta offers twice as great a probability of giving correct information concerning the condition of the child as a positive Wassermann reaction on the part of the mother.

5. The possibility of spermatic infection and the admissibility of Colles' law have not yet been conclusively proved or disproved. Williams believes such a possibility is supported by: (1) Conversion of a positive maternal reaction into a negative reaction after delivery without the administration of anti-syphilitic treatment. It must be borne in mind that such a positive reaction may occasionally be a manifestation of the establishment of an active immunity on the part of the mother against a syphilitic product of conception. (2) Clinical evidence. A case of probable superfecundation is described, in which a woman had intercourse with her husband and also with a syphilitic patient. One of the double ovum twins showed at necropsy visceral changes of congenital syphilis and a syphilitic placenta; the other twin and its placenta were apparently normal. The mother gave no evidence of a syphilitic infection, and several preceding pregnancies had resulted in the birth of normal children. (This case occurred in pre-Wassermann days.)

ZIMMERMANN, Baltimore.

UEBER LICHENOID ERUPTION BEI PYODERMIE (LICHEN PYODERMICUS) (LICHENOID ERUPTION WITH PYODERMIA [LICHEN PYODERMICUS]). HANS T. SCHREUS and ELIZABETH GOEHL, Dermat Ztschr. **31**:273, 1920.

The authors, and Prof. E. Hoffmann, in whose service the work was done, believe that they have observed a new, or at least heretofore undescribed, syndrome. Two children, 12 and 15 years old, respectively, presented eruptions on the skin made up of isolated pustular lesions from needle head to linseed

size, which were on the borders of an isolated single five-mark piece size lesion on the left cheek which (in one child), was covered by a brown crust under which there was an accumulation of pus on an eroded base. Some pustules were on the ear, on the borders and in the hairy portion of the scalp. The buttocks, the abdomen and the flexors were covered with large and small reddened follicular papules. Some of these were capped by a small crust, others had a central depression. They were lichenoid and were distributed singly and in groups. The face and extremities were free. The mucous surfaces were also free. The older child had a red surface for the lesions, and to the feel there was some suggestion of the nutmeg-grater surface. The temperature was slightly raised.

The differential diagnosis, according to the authors, ruled out trichophytosis with secondary lichen trichophyticus because of the absence of the organisms, and the character of an intracutaneous test. In one of the cases lichen scrofulosus was ruled out on account of lack of confirmatory findings of tuberculosis either in the lungs or on von Pirquet tests. The course of the disease also aided in the differentiation as the pyoderma soon cleared up. In the second case the suggestion of scarlet was slight. Papular syphilis was excluded by negative Wassermann and Sachs-Georgi reactions.

The lesions cleared without local therapy, and it is believed that this is proof that the eruption was more in the nature of an exanthem, and the "Allergie" phenomenon is called on to explain some of the facts.

As a sort of addenda, the observations of the authors are recorded that the complement-fixation test in furunculosis is more often positive after roentgen-ray treatment, and that the same holds true for trichophytosis. Perhaps the destruction of the organism in each instance increases the complement-fixing power.

GOODMAN, New York.

SUR UN CAS D'EPIDERMOLYSE BULLEUSE CICATRICIELLE A CYSTES EPIDERMQUES (REGARDING A CASE OF CICATRICAL EPIDERMOLYSIS BULLOSA WITH EPIDERMAL CYSTS). J. MONTPELLIER and A. LACROIX, *Ann. de dermat. et syph.* **12**: 575, 1920.

A native Algerian, 28 years of age, stated that he had had the disease for only a year, but he had been treated for trichiasis three years previously. This fact and the amount of atrophy present suggested to the authors that the duration was probably several years. There had been no trace of the disease in any member of the family.

Clinically the picture was classical, with bullae in various stages, small cysts and atrophy; Nicolsky's sign was positive on the skin of the extremities but not of the trunk.

Fortunately, five biopsies were obtained, and the histologic reports are given in detail. Bullae in all stages, the dystrophic skin and the epidermal cysts were studied thus. It was found that the roof of each bulla consisted of the whole epidermis, separated entirely from the derma. Secondary infection was frequent, and this dermal inflammation gave rise to a cicatrix. It is emphasized that there were no preexisting epidermic lesions to account for the formation of bullae, the real cause being probably a defect in adherence between derma and epidermis. It is thus different from pemphigus, which seems to show a special fragility of the epidermis, and from epidermolysis hereditaria traumatica, in which the splitting also occurs within the epidermis itself.

The study of the cysts is interesting. They appear only at the sites of previous bullae, and are found beneath the roofs of these bullae. They probably develop from the sebaceous apparatus which has been severed from the overlying epidermis by the formation of the lesions and undergoes cystic degeneration. The sweat glands, on the other hand, do not all atrophy, for in the case presented there was a considerable hyperhidrosis of the palms and soles.

PARKHURST, New York.

SECOND IMPROVED METHOD FOR DEMONSTRATING SPIRO-
CHAETA PALLIDA IN THE TISSUES. ALFRED SCOTT WARTHIN and
ALLEN C. STARRY, J. A. M. A. **76**:234 (Jan. 22) 1921.

Warthin and Starry present a method which they consider as great an improvement on the first method proposed by them as that was on the older methods, in that it possesses these advantages: 1. The time is much shortened; the entire procedure may be carried out in less than one hour after the sections have been mounted on cover-glasses. 2. The results are more certain. Spirochetes have been demonstrated in tissues in this method when all others have given negative results. Tissues are fixed in neutral formaldehyd, embedded in paraffin. Sections are cut and mounted on cover-glasses with albumin fixative. The paraffin is removed with xylene, alcohol and water. Next the cover-glass is rinsed with the section in 2 per cent. silver nitrate; the wet section is covered with another clean cover-glass, so that they are held together by capillary attraction; then they are placed carefully in a bottle of 2 per cent. silver nitrate and placed in an incubator for from thirty minutes to an hour. They are removed from the silver nitrate and the cover-glasses are separated. The cover-glass with the section is then placed in this reducing mixture:

	C.c.
Two per cent. silver nitrate solution.....	3
Warm glycerin	5
Warm 10 per cent. aqueous gelatin solution.....	5
Warm 1.5 per cent. agar suspension.....	5
Five per cent. aqueous hydroquinone solution.....	2

After the section is reduced, it is removed and rinsed in 5 per cent. sodium thiosulphate (hyposulphite) solution; rinsed in distilled water and mounted—absolute alcohol, xylene, balsam. The method is described in detail.

WAUGH, Chicago.

SUR UNE FORME ERYTHRODERMIQUE DU LYMPHOGRANULOME
BENIN (CONCERNING AN ERYTHRODERMIC FORM OF
BENIGN LYMPHOGRANULOMA). J. SCHAUHMANN, *Ann. de dermat. et*
sypht. **12**:561, 1920.

A clerk, 36 years of age, first noticed the presence of a palpable epitrochlear lymph node at the age of 14 years; at 15 he had a "bronchial catarrh" of three weeks' duration, and at 24 a troublesome cough which was readily overcome. In 1914 the first cutaneous manifestation appeared as a red spot on the scalp which persisted in spite of local applications. In 1917, similar spots began to appear on the legs, where they soon became confluent in places. The lesions have since come and gone insidiously, always with a predilection for the extensor aspects of the extremities.

An examination, made in May, 1917, showed the presence of large and small erythematous plaques, noninfiltrated and covered by a slight dry scale.

There were no subjective sensations or malaise. Some lymphadenopathy was noted, especially in the mediastinum; the spleen was enlarged and the liver was involved. The differential blood count showed a percentage of large mononuclear lymphocytes that varied between 8 and 11.

Biopsies were taken from the scalp, the leg and an epitrochlear lymph node, and the sections resembled in structure the miliary lupoid of Boeck. A complete histologic report is given.

It seems that just as we may have tumors or erythrodermas in leukemia and pseudoleukemia, and may encounter either the macular or the nodular form of leprosy, there are also two varieties of lymphogranuloma, the erythrodermic and the tumor-forming. What conditions determine the appearance of one or the other? Perhaps the virulence of the agent and the condition of the soil.

PARKHURST, New York.

RELATIVE EFFECTIVENESS OF VARIOUS FORMS OF TREATMENT IN NEUROSYPHILIS: OBSERVATIONS OF THE COMPARATIVE VALUE OF ROUTINE INTRAVENOUS TREATMENT, SPINAL DRAINAGE AND ARSPHENAMIZED SERUM INTRASPINALLY (SWIFT-ELLIS). JOHN H. STOKES and EARL D. OSBORNE, J. A. M. A. **76**:708 (March 12) 1921.

Twenty-five patients with neurosyphilis were placed on routine treatment and in conjunction received spinal fluid drainage of from 30 to 70 c.c. at weekly intervals. The average number of spinal fluid withdrawals in each case was five. After this treatment had been completed, two of the patients gave negative spinal fluid Wassermann reactions and in six a reduction in the number of lymphocytes was observed.

On the other hand, ten of these patients (some months after completion of the combined drainage and routine treatment) were given the Swift-Ellis-Ogilvie form of intraspinal therapy. The average number of intraspinal injections given was five. At the completion of this number of treatments, five patients showed a complete reversal of the spinal fluid Wassermann reaction to negative as compared with two after drainage. A reduction in the cell count to 11 or below was also noted in these five patients.

On comparison with cases of patients with neurosyphilis which were treated by routine intravenous arsphenamin and either mercurial inunctions or injections of soluble salts of this drug, no advantage was noted when drainage of the spinal fluid in addition to this medication was performed.

Stokes and Osborne make no pretense at setting forth final conclusions in the matter, but their experience leads them to the belief that spinal drainage has no superiority over an equal amount of routine treatment without drainage, and that arsphenamized serum given intraspinally appeared to produce more satisfactory and more permanent results.

MICHAEL, Houston, Texas.

THE VALUE OF THE CULTURAL METHOD IN THE DIAGNOSIS OF CHANCROID. OSCAR TEAGUE and OLIN DEIBERT, J. Urol. **4**: (Dec.) 1920.

Owing to the fact that the Ducrey bacillus loses its characteristic chain arrangement on passing from the tissue into the purulent discharge of the ulcer, it is difficult to make a definite diagnosis of chancroid by examination of smears of pus. Accordingly Teague and Deibert have devised a rapid and

successful method of diagnosis of chancroid by culture. Clotted rabbit's blood is used as the culture medium. Results can be obtained in 12 to 24 hours. In 274 cases with sores on the penis, for the most part unselected, 104 yielded cultures that were positive for the Ducrey bacillus. On the 134 negative cases, satisfactory notes were made on only 69. Of these 42 almost surely were patients with chancres, 8 had erosions or herpes; 8 had sores almost healed; 5 had sores that in all probability were nonvenereal, and only 6 were recorded at the time of culture as "probably chancroid." In view of these findings, the authors feel that their method of culture yields a diagnosis of chancroid in a large percentage of cases—probably above 90 per cent.

The authors do not claim that the methods are entirely new, but they demonstrate for the first time that the culture procedure is a practical method for the diagnosis of chancroid.

SENEAR, Chicago.

RECTAL INJECTIONS OF MASSIVE DOSES OF NEO-ARSPHENAMIN.

H. G. MEHRTENS, J. A. M. A. **76**:574 (Feb. 26) 1921.

The difficulty or impossibility in occasional instances of administering arspenamin and neo-arsphenamin by the intravenous route, as well as the desirability of finding a simpler method for their use in children, has led Mehrtens to investigate the value of rectal injections of these drugs. Previous investigations of the value of this method have been contradictory, but it was conceivable that the smaller doses used in the earlier studies were responsible in part, at least, for the poor results obtained.

The author has found it possible to give 4 gm. of neo-arsphenamin by rectum without appreciable ill effects. Arspenamin was so irritating by this route as to cause its abandonment. Neo-arsphenamin was prepared as for intravenous injections. The volume of each dose was 100 c.c.

One hundred and twenty-five patients have been treated in this manner. Nearly all were tabetic or cerebrospinal syphilitic patients, and therefore the clinical results cannot be evaluated properly at this time; but the improvement was at least as rapid as that observed when the intravenous method was used. This applies equally to the spinal fluid findings. Determinations of the arsenic content of the blood, spinal fluid and urine were made. Arsenic persists longer in the blood after the rectal method with large doses than after intravenous introduction. Approximately the same concentration in the spinal fluid was found with either method. Three times as much arsenic was excreted in the urine following rectal injection than by the venous route.

The author incidentally mentions that while arspenamin was being used in the irritating doses two long standing cases of pruritus were apparently cured.

Rectal injections of large doses of neo-arsphenamin have a place in therapeutics.

MICHAEL, Houston, Texas.

ZUR FRAGE DER PRAKTISCHEN BRAUCHBARKEIT DER AUSFLOCKUNGSREAKTION NACH SACHS-GEORGI (CONCERNING THE PRACTICAL VALUE OF THE SACHS-GEORGI REACTION). ELSBETH JACOB. Dermat. Ztschr. **31**:287, 1920.

Jacob concludes that the only reaction which is to be considered for practical work is the second modification of Sachs-Georgi, the reading after incubation for from eighteen to twenty hours. The results when properly read, from properly prepared antigen with good clinical controls are in accord with

the history and physical findings. In early primary syphilis the result is positive earlier, and in improperly or incompletely treated syphilis the positive result remains longer than the positive results in the Wassermann reaction. False strong positives were not encountered with the Sachs-Georgi reaction. The percentage of weak and nonspecific positives was hardly larger than with the Wassermann reaction. The Sachs-Georgi reaction in the hands of a well trained investigator becomes a welcome addition to the Wassermann reaction in the study of clinical material from a skin clinic or practice. The final conclusion is a broad one: The Sachs-Georgi is identical with the Wassermann reaction.

Reference to other abstracts of papers on the Sachs-Georgi reaction have led to the belief that the reactions complement each other, and that as yet the more recent test cannot stand alone. Levinson and Peterson "are of the opinion that the Sachs-Georgi reaction offers a valuable aid in the routine examination for syphilis when used in conjunction with the Wassermann reaction."

(The reader is advised to review the paper by Levinson and Petersen, "The Sachs-Georgi Reaction for Syphilis," which appeared in the March number of the ARCHIVES OF DERMATOLOGY AND SYPHILOLOGY, page 286 and a paper by Logan on the "Sachs-Georgi Test," *Lancet* 1:14, 1921. These are the only two papers [other than abstracts] in English on this subject.)

GOODMAN, New York.

LE SERO-DIAGNOSTIC DE LA SYPHILIS (THE SERODIAGNOSIS OF SYPHILIS). L. SPILLMANN and P. LASSEUR, *Ann. de dermat. et syph.* 11:507 and 12:586, 1920.

Realizing that while many authorities place a high estimate on the value of the Wassermann reaction, others consider it dangerously uncertain, the writers seek to point out the chief causes of error. In the first place, the operator must be thoroughly familiar, not with the Wassermann reaction alone, but with biologic reactions in general. He must familiarize himself with the work of the pioneers in this field.

With the aid of algebraic formulae the quantitative and qualitative variations of the reaction are explained. The physicochemical factors are considered and many points of caution in technic are mentioned. The matter of antigens is discussed and the use of cultures of *Spirochaeta pallida* in this rôle, which is thought inadvisable on account of their variability. The work of Vernes in the direct measurement of flocculation is mentioned.

Concluding, the authors refer to their results in a series of cases to prove the true value of the reaction: they cite a number of individual cases also. In experienced hands the results are well within the allowable limits of experimental error, and acknowledging it to be imperfect, we are advised to avail ourselves of its valuable aid, always considering it merely as one of the signs, until some better test may be devised. Its use is recommended (1) as a diagnostic factor in difficult cases, (2) as a guide in treatment and (3) in prognosis.

PARKHURST, New York.

THE TREATMENT OF RHINOPHYMA BY THE DESICCATION METHOD. W. L. CLARK, *Urol. & Cutan. Rev.* 25:63 (Feb.) 1921.

The author has treated ten patients with rhinophyma by this method and reports satisfactory results. The cosmetic effect is superior to that obtained when simple excision is practiced.

After the enlarged follicles have been emptied as thoroughly as possible, the tissue is anesthetized with procain and epinephrin. The hypertrophic area is then desiccated as deeply as necessary and pared off with a sharp scalpel or razor until the nose is restored to its normal size and shape. Only the most severe cases require paring; in those of moderate degree contraction of the scar tissue, which results from the desiccation, will suffice to restore the nose to approximately its normal size.

In four instances, there was improvement in the general health of the patients following this treatment. This may be attributed to the relief from focal infection seated in the infected follicles. One patient had an associated chronic, purulent bulbar conjunctivitis which was considered secondary to the infected sebaceous glands. This promptly cleared up after desiccation of the rhinophyma.

MICHAEL, Houston, Texas.

TWO CASES OF PSORIASIS TREATED BY DANYSZ' METHOD.

H. W. BARBER, *Proc. Roy. Soc.* **14**:24 (Feb.) 1921.

This report calls attention to the theory of Danysz discussed in his book ("Origine, Evolution et Traitement des Maladies Chroniques Non-contagieuses") that certain forms of eczema, urticaria, angioneurotic edema and certain other conditions, such as asthma, chronic albuminuria and many gastrointestinal disorders, are due to a state of "immunity anaphylaxis." The theory is supported by the fact that rabbits repeatedly injected with minute doses of foreign serum or bacterial protein for several weeks gradually develop chronic diseases of various kinds, such as arthritis, alopecia, paralysis, etc. The same is true of horses used for preparation of curative serums. Danysz attempts to counteract this anaphylactic state by daily injections of bacterial proteins obtained by autogenous fecal cultures. Thus the method is comparable to the nonspecific protein treatment. Two cases were presented that showed distinct improvement after twelve injections given on alternate days.

Guy, Pittsburgh.

INTOXICATIONS ET MORTS PAR LES ARSENOBENZENES—LEUR CAUSE (INTOXICATIONS AND DEATH FOLLOWING ARSPHENAMIN—THEIR CAUSE). C. LAURENTIER, *Ann. de dermat. et syph.* **1**:38, 1921.

A young man, two days after receiving 0.75 gm. of neo-arsphenamin, developed symptoms of extreme irritation of the central nervous system and albuminuria. In four days both disappeared. A second patient received the same amount of the same preparation, and two days later he developed extreme nervous symptoms as well as an acute retention of urine. Necropsy examination revealed only pulmonary edema.

In 1918, in Audry's service, 0.75 gm. of a neo-arsphenamin preparation was administered to each of five patients. Three reacted violently the next day, but recovered. The other two, between fifty-two and fifty-eight hours after treatment, developed eclamptic symptoms with a lethal exitus. Necropsy examination revealed nothing of importance.

It has been noticed that accidents follow the use of a new series of ampules, erythematous manifestations being frequent and icterus rare in the author's experience. Of course, the other accepted causes of accidents are undeniable, but the drug itself seems often to be at fault, and the chemists have further work to do with this in mind.

PARKHURST, New York.

URTICARIA UND SAEUREWIRKUNG (URTICARIA AND ACID ACTION). VIKTOR KOLLERT, *Dermat. Ztschr.* **31**:281, 1920.

It is admitted that the lymph plays an important rôle in the formation of the urticarial wheal. Experimentally and otherwise this has been confirmed. Concerning the cause of the control of the local edema, opinion is divided. The author has made certain observations which lead him to believe that acids may be the cause of the urticaria manifestation. Among his patients he found that the eating of apples caused urticaria in four cases. The acids of the apple were held responsible. As a further confirmation of the acid idea, he advances the observation that urticaria in women during menstruation and in the early months of pregnancy is more frequent, and that dermatographism is more readily evoked than at other times. The supposed increase of acidity at these times is held responsible. Many other reasons to believe that acids are the cause of urticaria are advanced; for example, the urticaria following the injection of acid arsphenamin. Before closing his paper, however, the author insists that he must not be misunderstood, and that he does not hold the acids alone responsible, but rather a disturbance of ion concentration. The treatment of urticaria advised is, of course, the use of alkalies.

GOODMAN, New York.

GRANULOMA INGUINALE. M. F. CAMPBELL. *J. A. M. A.* **76**:648 (March 6) 1921.

Five cases of this disease, occurring in the urological service of Bellevue Hospital, are reported. Two of these five cases have been previously described by Symmers. All of the patients were native, male negroes. The cell inclusions of Donovan were demonstrable in four of the cases. The organism seems to bear direct etiologic relationship to the disease. It likewise seems probable that it is a secondary invader, promoting the process of ulceration.

Three of the patients presented chronic, ulcerating granulomas of the genitals and groin. One patient had the rare elephantiasis variety affecting the scrotum. The clinical features of one case are not described.

Tartar emetic was administered intravenously to each patient. One was cured, three were improved but discontinued treatment prematurely, and one patient died. Death resulted from sepsis due to infection of the involved scrotum (case with elephantiasis variety).

The author believes that the disease is endemic in this country and occurs with greater frequency than published reports would indicate. The diagnosis of granuloma inguinale must be entertained in all chronic ulcerative lesions of the genital and perigenital regions; especially if the patient is a negro native of the Southern states or tropical countries. The intravenous administration of tartar emetic constitutes a specific treatment.

MICHAEL, Houston, Texas.

SULL 'ACARIASI DA GRANO (GRAIN-ITCH DERMATITIS). D. MAJOCCHI, *Gior. ital. d. mal. ven.* **61**:709 (Dec.) 1920.

The author describes several cases of a universal vesiculo-erythematous dermatitis. In all of the patients, as well as in their clothes and in samples of wheat and flour, Majocchi found the *acaros tritici* or *pediculoides ventricosus*. Cases of this disease were recognized in Italy for the first time in 1908 by Ducrey. They appear in epidemic form. At present the infected dis-

tricts are the provinces of Romagna, Ravenna, Forli, Ferrara, Modena and Bologna. The eruption is always erythematopapular in the beginning, rapidly developing into vesicular. The author describes the pure papular or acneiform variety, the urticarial and the hemorrhagic. Infection by common organisms produce the secondary or pyodermal forms. The general health remains unimpaired. The patients were quickly cured with Wilson's ointment.

PARDO-CASTELLO, Havana.

STIGMATA OF PREDISPOSITION TO BONE AND JOINT TUBERCULOSIS. W. C. RIVERS, Brit. J. Child. Dis. **202-204**:179 (Oct.-Dec.) 1920.

Continuing his article, which was begun in the previous issue of this journal (p. 148), the author reports, among other signs, the apparent relative frequency of the occurrence of abundant long silky lanugo hairs on the backs of tuberculous children. It seems equally frequent in boys and girls, having been found in 3 out of 130 boys (2.3 per cent.) and in 3 girls among 116. In a control of 181 normal schoolboys it was seen only once (0.5 per cent.), and then in a degree far less than in any of the tuberculous cases. It is thought to be an atavism. Among the conclusions emphasis is laid on the importance of the atavistic qualities, including ichthyosis and pigmentation, and it is urged that no tuberculous ichthyotic patient, unless of great intellectual parts, and no tuberculous mentally defective person should be allowed to reproduce.

PARKHURST, New York.

REPORT OF A CASE OF ANAPHYLAXIS FOLLOWING AN INTRADERMAL PROTEIN SENSITIZATION TEST. J. GERSTENBERGER and J. H. DAVIS, J. A. M. A. **76**:721 (March 12) 1921.

The patient was an infant, aged 12 months, who had a mild dry eczema of the face, chest and arms and a decided emphysema accompanied by wheezing and a somewhat labored respiration. An enlarged thymus was demonstrated by fluoroscopy. Cutaneous scratch tests proving negative, it was decided to try intradermal protein sensitization tests.

While egg yolk allergen and egg albumin were being injected, the child developed cyanosis and dyspnea of marked degree. Epinephrin was administered with relief of the symptoms. The next day urticarial wheals appeared. Two days later the tests were again performed, but with different proteins. No untoward effects occurred.

Three days after the second test, another was made. Only egg yolk allergen was injected. Within a few minutes the child became extremely cyanotic and dyspneic, and death would probably have occurred had not a large dose of epinephrin been promptly administered. At the site of injection of the protein a large wheal developed in each test that was followed by symptoms of anaphylactic shock.

MICHAEL, Houston, Texas.

ZUR SPEZIFISCHEN BEHANDLUNG DER TIEFEN TRICHOPHYTIE (SPECIFIC TREATMENT OF DEEP TRICHOPHYTOSIS). MAXIMILIAN STRASSBERG, Wien. klin. Wchnschr. **34**:60, 1921.

Patients with deep trichophytosis of the head have been variously treated with trichophytin, along the lines of tuberculin treatment. It has been found that injections which provoke chills and fever are the ones that produce the best results on the trichophytosis. Injections so graded that they do not pro-

duce reactions are not efficacious. It has also been found that injections of tuberculin that produce reactions can speedily cure trichophytosis, in other words, nonspecific therapy. In other cases milk injections produced good therapeutic results after a series of trichophyton injections had failed either therapeutically or to produce reactions on injections.

GOODMAN, New York.

TOPICAL APPLICATIONS OF RADIUM. H. H. BOWING, Am. J. Roentgenol. **7**:582 (Dec.) 1921.

The terms milligram hours, erythema dose and distance screening are defined as they are used at the Mayo Clinic.

In treating cancer of the breast with or without metastasis a thorough radiation is indicated before operation and radiation after operation as soon as convalescence permits. In recurrent carcinoma of the breast improvement has been noted in all cases. Deep roentgen-ray treatment is given in addition to radium applications. Round cell sarcoma responds readily to combined radium and roentgen-ray therapy. Melanotic sarcoma is hardly influenced by this kind of treatment. The simple type of tuberculous adenitis offers the best result. If suppuration is present, surgical measures may be necessary. Remissions were obtained by radium therapy in practically all cases of splenomyelogenous leukemia. Details of treatment are given.

MICHAEL, Houston, Texas.

QUELQUES MERITES COMPARES DE L'ARSENOBENZOL ET DU MERCURE (A COMPARISON OF THE MERITS OF ARSPHENAMIN AND MERCURY). SABOURAUD, Presse méd. **28**:533 (Aug. 4) 1920.

Interruption of treatment by military service has made it possible for Sabouraud to examine syphilitic patients who had been treated exclusively with either arsphenamin or mercury. Patients who had been subjected to a long course of mercury, especially in the form of gray oil, never showed a relapse to a positive Wassermann reaction. All cases in which it had become negative during the course of treatment with mercury remained so. On the other hand, patients inefficiently and exclusively treated with arsphenamin showed a greater degree of fixation at the time of reexamination than at the time when treatment was interrupted. Sabouraud emphasizes the fact that mercury still holds an important position in antisymphilitic therapy, especially in patients with an infection of some duration.

ZIMMERMANN, Baltimore.

ALEUKEMIC LEUKEMIA WITH UNUSUAL SKIN MANIFESTATIONS: REPORT OF CASE. M. A. BLANKENHORN and H. GOLDBLATT, J. A. M. A. **76**:583 (Feb. 26) 1921.

The patient presented a profuse, generalized eruption composed of various sized, purpuric, infiltrated patches in different stages of evolution and involution. The mouth and conjunctivae were involved. Subjective symptoms are not mentioned. There was a moderate general adenopathy and enlargement of the liver and spleen. Blood counts did not show the abnormal leukocytosis characteristic of lymphatic leukemia. Blood cultures were positive for *Staphylococcus albus*. The temperature ranged from 99 to 103 F., and there were other indications of a generalized infection.

Biopsy showed a dense infiltration of the corium with large and small lymphocytes and atypical endothelial cells. At necropsy, the report of which is given in detail, the features of lymphatic leukemia were observed.

MICHAEL, Houston, Texas.

DEUX CAS DE LEISHMANIOSE CUTANEE CONTRACTEE EN ESPAGNE ET EN FRANCE (TWO CASES OF ORIENTAL BOIL CONTRACTED IN SPAIN AND FRANCE). P. RAVAUT, *Ann. de dermat. et syph.* **1**:29, 1921.

Neither patient had been outside of France or Spain, but laborers from northern Africa had lived in their vicinity. The bites of flies or mosquitoes are blamed.

Although the Leishman bodies, intracellular and extracellular, were found in large numbers, neither case was clinically typical. The evolution was slow, and both patients responded favorably to several weekly injections of neo-arsphenamin with 0.3 gm. as a minimum dose. The second patient responded slowly, however, and the intravenous use of tartar emetic is proposed as a better measure.

This is the first reported case of contagion in France.

PARKHURST, New York.

THE TREATMENT OF NEUROSYPHILIS BY THE INTRASPINAL ROUTE WITH THE REPORT OF A CLINICAL STUDY OF A SERIES OF CASES TREATED FROM THE POINT OF VIEW OF INCREASED PERMEABILITY OF THE MENINGES. KEIDEL and MOORE, *Johns Hopkins Hosp. Bull.* **31**:404 (Nov.) 1920.

With the idea of increasing the effectiveness of treatment of neurosyphilis, the authors administered an intraspinal injection of mercurialized serum (Byrnes) and twenty-four hours later an intravenous injection of arsphenamin. In this way a maximum concentration of arsenic was obtained in the blood stream at the time of maximum meningeal irritation. Such treatments were given in courses usually of six treatments administered one each week, and each course was followed by ten to twelve weeks of administration of mercury by inunctions.

As judged by the treatment of twenty-five cases of neurosyphilis, this method did not yield as good results as the Swift-Ellis method. The authors conclude that the mode of action of intraspinal medication does not depend on increased permeability of the meninges, and that aseptic meningitis produced by intraspinal injection of irritants may prove an untoward, rather than a beneficial, factor in the treatment of neurosyphilis.

ZIMMERMANN, Baltimore.

TRANSMITTED CONGENITAL SYPHILIS. D. H. PATERSON, *Brit. J. Child. Dis.* **202-204**:197 (Oct.-Dec.) 1920.

A case is reported as another proof that a mother with congenital syphilis may transmit it to her child. The disease had been transmitted from the maternal grandmother to her daughter, who gave birth to a syphilitic child, the patient. This child, a boy aged $2\frac{1}{2}$ years, was mentally deficient, and presented the characteristic facies of congenital syphilis. The Wassermann reaction was positive. A photograph of the mother is reproduced, showing a saddle nose and external strabismus. She showed an old interstitial keratitis

and her Wassermann reaction was + + +. The boy's father and another baby aged 2 months both gave negative Wassermann reactions and were apparently nonsyphilitic. The maternal grandmother had died of tabes.

(Another case was recently reported by Bruusgaard [*Acta Dermat.-Vener.* **1**:1, 1920] in the *ARCHIVES OF DERMATOLOGY AND SYPHILOLOGY* **2**:771 [Dec.] 1920.)

PARKHURST, New York.

JUVENILE TABES. C. ROSENHECK, J. A. M. A. **76**:572 (Feb. 26) 1921.

The author discusses the history and symptomatology of this condition and reports a typical case. In 40 per cent. of the reported cases the onset was characterized by visual difficulty. Next in frequency lancinating pains, bladder disturbances and gait defects were encountered. The average age of onset was 15 years; the youngest patient was 3 years of age.

Rosenheck's patient was a girl, aged 18 years, born of apparently healthy parents. Three years previously severe lancinating pains made their appearance, followed in two years by paresthesias and later by slight ataxia. In addition to markedly unequal and fixed pupils, there were: absent deep reflexes, positive blood and spinal fluid Wassermann reactions, increased globulin, 130 cells per cm., and a colloidal gold reading of 5544334555.

MICHAEL, Houston, Texas.

HEREDITARY HEMORRHAGIC TELANGIECTASIA WITH RECURRING (FAMILIAL) HEREDITARY EPISTAXIS. H. I. GOLDSTEIN, *Arch. Int. Med.* **27**:102 (Jan.) 1921.

The literature on this rare disease is thoroughly reviewed by the writer. Many cases are reported in which the condition was accompanied by telangiectasis without hemorrhages and vice versa. The lesions in hereditary cases are more pronounced and numerous toward middle life and are most commonly found on the face and fingers. There is no change from normal in clotting and bleeding time and no history of hemophilia. Many remedies are recommended for the bleeding, but treatment is not satisfactory. The usual methods of treating telangiectatic lesions are given. A report of the author's cases is also given in detail—eleven patients in one family.

JAMIESON, Detroit.

RADIUM AND NEVUS. ROBERT ABBE, *Urol. & Cutan. Rev.* **25**:65 (Feb.) 1921.

Abbe's long experience in the use of radium leads him "to deprecate the enthusiastic claims of many who are newly possessed of radium, that the treatment of a naevus constitutes one of the most successful fields of radium service." In portwine mark, restoration of the exact normal tint of the skin is not obtainable. In treating nevi with radium it is necessary to cause erythema, but not to blister. This dose is a good guide to treatment.

After the first dose an interval of six weeks should be allowed to observe the effect, and an additional six weeks before another treatment is given. Thus nevi are treated at intervals of three months for at least two years. It is essential in treating cavernous angioma that pressure sufficient to cause apposition of blood vessel walls is maintained throughout the exposure. In portwine marks the plaque should be moved about during the sitting or the end-result will be spotty.

Abbe has found ignipuncture an efficient method for destroying radium telangiectases. He uses a lady's hat pin heated to a cherry red in a flame and introduced at a black heat into the most prominent point of each little vein.

MICHAEL, Houston, Texas.

TROIS CAS DE CONTAGION SYPHILITIQUE AU PASSAGE (THREE CASES OF SYPHILITIC CONTAGION DURING BIRTH). S. LOMHOLT, Ann. de dermat. et syph. **1**:17, 1921.

The mothers had all acquired syphilis during the last months of pregnancy and had presented the first generalized eruption of the disease about the time of confinement, with lesions on the genitalia. Each infant developed multiple ulcerations of the scalp, which had been the presenting part, and the presence of *Spirochaeta pallida* was easily demonstrated. The regional lymph nodes were enlarged. No signs of congenital syphilis were present, and in one case the Wassermann reaction at first was negative.

PARKHURST, New York.

FAUT-IL TRAITER LA FEMME ENCEINTE D'UN SYPHILITIQUE (SHOULD ONE TREAT THE PREGNANT WIFE OF A SYPHILITIC)? CARLE, Ann. de dermat. et syph. **1**:23 1921..

The author has long held that such a woman should receive treatment only if a clinical and serologic examination shows that she is syphilitic. In his practice he has found this plan to be a good one, having used it extensively.

Only in certain cases is it thought advisable that the husband confess his disease to his wife, or that she be told by the physician, for this often produces domestic trouble. It is customary to examine her under some pretext, keeping her in ignorance of the real purpose in view.

If the woman be syphilitic, it is urged that the treatment be intensive.

PARKHURST, New York.

THE REACTIONS OF THE ARSINES. PRELIMINARY PAPER. CONDENSATION OF PRIMARY ARSINES WITH ALDEHYDES. ROGER ADAMS and CHARLES S. PALMER, J. Am. Chem. Soc.

In an attempt to discover some substance with a higher therapeutic value and more particularly with greater stability than arsphenamin, the authors have studied the condensation of aldehyds with phenylarsin. Addition products are formed between two molecules of aldehyd and one molecule of arsin. Up to the present time benzaldehyd and butyraldehyd have been condensed with phenylarsin, and it seems probable that this reaction may be extended to any aromatic or aliphatic arsins and aldehyds. The compounds are perfectly stable in cold water, 10 per cent. sodium hydroxid solution or dilute hydrochloric acid. The compounds already made are not soluble in water, but it is hoped to obtain certain derivatives in this series which will be soluble in water and capable of therapeutic testing.

SENEAR, Chicago.

TESTS FOR CHANGES IN THE PROTEIN CONTENT OF THE CEREBROSPINAL FLUID, BASED ON THE FLOCCULATION OF LIPOIDS. H. NOGUCHI, J. A. M. A. **76**:632 (March 6) 1921.

None of the present methods for determining pathologic changes in the protein content of the cerebrospinal fluid is without disadvantages. They are either unsatisfactory from the standpoint of technic or because of failure to differentiate the normal from the pathologic.

The proposed method is not altogether based on the direct precipitation of the proteins contained in the cerebrospinal fluid, but is due to a concomitant flocculation of certain lipoids which are present in the reagent. The reagent consists of two components: (1) an alcoholic extract of acetone-insoluble tissue lipoids, and (2) an acid-salts solution. Methods of preparation are given in detail. Comparative observations show that the test runs parallel with the butyric acid reaction. The test is simple, and the result can be read within ten minutes.

A subsequent article will describe its use in quantitative determinations of the protein content of the cerebrospinal fluid.

MICHAEL, Houston, Texas.

ETIOLOGY OF ACNE ROSACEA THROUGH A VISCERO-NEURO-LOGIC MECHANISM. F. P. MILLER, *Am. J. M. Sc.* **161**:120 (Jan.) 1921.

In this article the writer shows, in a rather complex statement which cannot well be abstracted, that the rosacea of this disease may be due to a mechanism of the nervous system through stimulation of the sensory division of the fifth cranial nerves, the stimulation arising from irritation which may be either from within or without the body. Activity of the psychic centers by repeatedly producing the phenomenon of blushing is also stated to be an etiologic factor in that this gradually produces chronically enlarged venous capillaries. The acne lesions proper he regards as mere secondary manifestations.

JAMIESON, Detroit.

A STUDY OF THE BEHAVIOR OF SYPHILITIC AND NORMAL SERA TOWARD CERTAIN COLLOIDAL SOLUTIONS. MASON, *Johns Hopkins Hosp. Bull.* **31**:234 (July) 1920.

The following reagents were used: (1) 0.3 c.c. of inactivated undiluted serum, (2) 0.4 c.c. of alcoholic extract of beef heart plus 0.2 per cent. of cholesterin, diluted 1:6 with physiologic saline, and (3) 0.6 c.c. 8 per cent. sodium chlorid solution. The mixture was incubated at 37 C. for from twelve to sixteen hours, and the presence or absence of flocculation determined. The results obtained by this method with 200 serums corresponded in 95 per cent. of the cases to those obtained with the Wassermann test of the same serums.

ZIMMERMANN, Baltimore.

BRIEF CONSIDERATIONS ON SURGICAL TUBERCULOSIS IN INFANTS. C. G. CUMSTON, *Brit. J. Child. Dis.* **202-204**:189 (Oct.-Dec.) 1920.

Among other manifestations, subcutaneous abscesses and subcutaneous gummas are considered. The author has found the abscesses to be of common occurrence in tuberculous infants, directly caused by the ordinary bacteria of suppuration having been fostered by a tuberculous soil. Usually multiple and disseminated over the body surface, these abscesses last for months. Sometimes they are limited to the scalp, the subungual, gluteal or malar regions.

The gummas are frequently encountered, scattered over the body or limited to the gluteal region or limbs. Although they do occur in infants from 6 months to 1 year of age, they are much more frequent after the first year of life.

PARKHURST, New York.

TREATMENT OF VASCULAR NEVI WITH RADIUM. D. W. MONTGOMERY and G. D. CULVER, Boston M. & S. J. **183**:412 (Sept. 30) 1920.

The authors report several cases of cavernous angioma in which excellent results were obtained by the use of radium. They give the technic of the applications in detail so that others may profit by their experience. They state that it is far better to err on the side of screening too much than too little. This precaution is particularly necessary when a cosmetic result is wished, as is so often the case in nevi. Nevus araneus is not amenable to radium treatment.

MICHAEL, Houston, Texas.

STUDIES IN THE VALUE OF WASSERMANN TESTS. I. FREQUENCY OF A POSITIVE WASSERMANN REACTION IN AN UNSELECTED MALE INDIAN POPULATION. K. R. K. IVENGAR, Indian J. M. Res. **7**:398 (Oct.) 1919.

The cases reported were taken from unselected, apparently healthy, male Indian population, coming for treatment to the Pasteur Institute. The cases dealt with in the article came from all classes of society, rich and poor, without any distinction to caste or religion. The age of the cases examined ranged from 20 to 60. Of the 400 cases examined, the reaction was found to be positive in eighty-eight cases or 22 per cent.

GUTIERREZ, Manila, P. I.

ANTIMONY IN LEPROSY. F. G. CAWSTON, Brit. M. J. **2**:855 (Dec. 4) 1920.

The author previously reported several cases of leprosy successfully treated with injections of antimony. In this article he reports two additional cases in which favorable results were obtained by giving a series of intramuscular injections with Oppenheimer's colloidal preparation of antimony (Oscal stibium). The dosage averaged from 2.5 cm. to 5 cm. given daily and then every other day.

OLIVER, Chicago.

ACNE VACCINE THERAPY. MARTIN F. ENGMAN, J. A. M. A. **76**:176 (Jan. 15) 1921.

Engman describes the types of acne best suited for vaccine therapy, also the dosage used to secure the best results. The author states that in his opinion the failure to obtain proper therapeutic results in the use of this method has been due to the administration of too large doses or too frequent administration of the vaccine.

WAUGH, Chicago.

CASE FOR DIAGNOSIS. S. E. DORE, Proc. Roy. Soc. **14**:13 (Jan.) 1921.

A child aged 9 developed deep seated scars leaving vesicles on exposed parts of the body, produced, it was thought, by the sun's rays and heat. A tentative diagnosis of hydroa aestivale was offered and a quinin ointment prescribed with an idea of intercepting the sun's rays.

GUY, Pittsburgh.

THE PHENOMENON OF VERNES AS APPLIED TO THE SERO-DIAGNOSIS OF SYPHILIS. LEON H. CORNWALL and LOUIS S. ARONSON, J. A. M. A. **75**:1697 (Dec. 18) 1920.

The authors assert that a study of these syphilitic indexes constitutes a measure of importance in treatment. The specificity of the reaction is vouched

for by Vernes after an extensive application to a large number of patients suffering from various diseases, which application has been controlled by the clinical observations of Marie, Landouzy, Chatelin and others.

CASE OF POST-VACCINAL PSORIASIS. GEORGE PERNET, *Proc. Roy. Soc.* **14:1** (Jan.) 1921.

Typical psoriasis developed in a 16 year old girl immediately following vaccination. Other members of the Society had seen psoriasis develop after vaccination or slight injury.

GUY, Pittsburgh.

A SUGGESTED NEW METHOD OF MEASURING X-RAY DOSAGE.

C. E. S. PHILLIPS, *Arch. Radiol. & Electroth.* **15:215** (Dec.) 1920.

The author is endeavoring to perfect a reliable means of accurately measuring roentgen-ray dosage. He hopes to develop an instrument that will register on a dial what is the actual or relative radiation intensity of a pencil of rays. The proposed scheme is based on the fact that a gas becomes a conductor of electricity when traversed by roentgen rays. Its essential feature consists in the use of a thermionic valve.

MICHAEL, Houston, Texas.

SIGNIFICANCE AND VALUE OF A POSITIVE WASSERMANN REACTION IN LEPROSY. K. R. K. IYENGAR, *Indian J. M. Res.* **7:407**, 1919.

Iyengar examined 100 cases of undoubted leprosy in which the ages of the patients ranged between 30 and 60. Of these 100 cases, thirty-four were of the nodular type; fifty-two of the anesthetic and fourteen of the mixed type. Positive reactions were obtained in seventeen, sixteen and eight cases, respectively, or 41 per cent.

The serums of twelve children born of leper parents was also examined. The ages of these ranged from 11 months to 15 years. All gave a negative reaction. They had not showed any signs of the disease.

GUTIERREZ, Manila, P. I.

CASE OF URTICARIA PIGMENTOSA WITH BULLOUS LESIONS.

J. M. H. MACLEOD, *Proc. Roy. Soc.* **14:17** (Feb.) 1921.

At the age of 3 months the patient developed an itching generalized, mixed macular and nodular eruption, new lesions appearing in crops at intervals since, the palms and soles only now being free of lesions. In addition to the usual lesions, there were present variously sized wheals, vesicles and bullae. The usual mast-cell infiltration was demonstrated in sections.

GUY, Pittsburgh.

KERATOSIS AND SKIN CANCER. Abstracted from the minutes of the meeting of the Section on Dermatology and Syphilis. *Med. J. of Australia* **2:** (Sept. 18) 1920.

The conclusion was reached at this meeting that these conditions were extremely common and that the incidence was greater in Australia in proportion to other cases than elsewhere. It was also pointed out that from 50 to

100 miles from the coast line the air was relatively devoid of moisture, and that certain types of people were predisposed to the condition.

GUTIERREZ, Manila, P. I.

A SHORT SILVER IMPREGNATION METHOD FOR THE DEMONSTRATION OF SPIROCHAETA PALLIDA IN TISSUE. S. R. HAYTHORN, J. A. M. A. **76**:725 (March 12) 1921.

A comparatively simple method is outlined which is said to give practically the same picture as that obtained by the Levaditi procedure. Only three days are required for the preparation of the tissue for study.

MICHAEL, Houston, Texas.

AN ANALYSIS OF OVER FIVE HUNDRED CASES OF GENITAL CHANCRES IN THE NATIVE MALE. H. P. HENNESY, Indian Med. Gaz. **55**:327 (Sept.) 1920.

The class of patients dealt with in this paper were of the coolie type, hence the lowest class. The patients with few exceptions were Malays or Indians. The age incidence is given in the following table; otherwise the article contains nothing of interest.

Under 20	20-30	30-40	Over 40
27	426	49	17

GUTIERREZ, Manila, P. I.

CASE OF EPIDERMOLYSIS WITH EPIDERMAL CYSTS. J. H. SEQUERIA, Proc. Roy. Soc. **14**:19 (Feb.) 1921.

A young man, aged 20, who had been incapacitated his entire life on account of epidermolysis bullosa, showed numerous atrophic scars, bullae and epidermal cysts.

GUY, Pittsburgh.

A CASE OF TROPICAL SORE CURED BY INTRAVENOUS INJECTION OF TARTAR EMETIC. T. D. BANA, Indian Med. Gaz. **55**:340, 1920.

The patient reported had nine boils. He had been under the care of various physicians and had been treated for syphilis. Bana gave him six intravenous injections of tartar emetic of $\frac{3}{4}$ grain each on February 12, 16, 19 and 23, and 1 grain on March 16 and 19. The patient made a progressive and uneventful recovery.

GUTIERREZ, Manila, P. I.

NOTES ON NOVO-ARSPHENAMIN RASH. MOHAN BOSE, Indian Med. Gaz. **55**:334, 1920.

The article contains nothing new to syphilographers.

GUTIERREZ, Manila, P. I.

AINHUM, A FAMILY DISEASE. K. M. B. SIMON, J. A. M. A. **76**:590 (Feb. 26) 1921.

The occurrence of this condition in a father and two sons is reported. No details are given.

MICHAEL, Houston, Texas.

THE FOURTH VENEREAL DISEASE, ULCERATION AND GANGRENOUS BALANOPOSTHITIS, WITH CASE REPORT. W. M. DONOVAN, Am. J. Med. Sc. **161**:267 (Feb.) 1921.

Report of a case, and a consideration of the known facts of the disease.

JAMIESON, Detroit.

SYPHILITIC RUPTURE OF A PAPILLARY MUSCLE OF THE HEART.

SPALDING and VON GLAHN, Johns Hopkins Hosp. Bull. **32**:30, (Jan.) 1921.

This article consists of the report of a case of syphilitic aortitis and aortic insufficiency with rupture of one pillar of the posterior papillary muscle of the left ventricle and demonstration of *Spirochaeta pallida* in one segment of the ruptured muscle.

ZIMMERMANN, Baltimore.

Society Transactions

SOCIETY OF DERMATOLOGY AND SYPHILOLOGY, MADRID

Meeting Held Feb. 4, 1921

DR. AZÚA in the Chair

CASE FOR DIAGNOSIS. Presented by DR. FERNANDEZ DE LA PORTILLA.

Nine months ago this boy had a hard chancre, which left a typical scar in the internal side of the foreskin. He had been given a complete course of silver arsphenamin, two courses of mercuric benzoate and one and one-half courses of neo-arsphenamin; one month after the last course of treatment, a lesion appeared on the penis next to the site of the first chancre; in the lesion Dr. Arcaute found spirochetes. Clinically the sore presented specific features, but it is doubtful whether it was a chancre or an ulcerative syphilid. The patient had not had sexual intercourse since acquiring syphilis; therefore the second infection must have been caused by spirochetes, which had become saprophytes and which had remained near the site of the first infection. They had evidently increased virulence and had caused a new chancre to develop. This case was interesting as the patient was treated with silver arsphenamin.

DISCUSSION

DR. AZÚA said he thought the condition was a nonprimary specific lesion.

DR. SÁNCHEZ COVISA said he thought the patient had secondary papules of chancrous form recurring from the previous infection.

DR. SAINZ DE AJA had seen patients in whom the lesion was not so infiltrated. He thought the condition was a recurrence of the previous secondary syphilis; to assume that it was a secondary infection from the patient himself was misleading and complicated matters.

DIPHThEROID HARD CHANCRE OF THE TONGUE. DR. CUBERO.

This interesting case was presented for diagnosis.

DR. BARRIO DE MEDINA said that from the information furnished by the patient he concluded that the lesion had been cauterized with copper sulphate two and three times a day for eight days. Therefore the infiltration was not significant, especially if considered with the fact that the submaxillary infarcts were not very plain. If Dr. Cubero had not found spirochetes the diagnosis is doubtful.

EPITHELIOMA AND RADIUM. DR. SAINZ DE AJA.

The patient, a woman with epithelioma of the back of the hand, had been presented at a previous session. She refused to consent to an operation and double radiations had been used in two twenty-four-hour cycles, each with

1 mm. of aluminum. There had been no improvement. This confirms the fact that epitheliomas of the hands present a far more serious prognosis than other epitheliomas.

For comparison, another patient was presented with pearly epithelioma of the lower right eyelid accompanied by conjunctival involvement, both ulcerated and infiltrated, cured in a fifteen-hour session with 1 mm. of aluminum; this was a great success especially in view of the marked palpebral infiltration and the extensive conjunctival involvement.

Another patient with epithelioma originating on a scar made by the roentgen-rays on a tuberculous lupus was receiving treatment. All these patients should receive surgical treatment from the beginning.

TREATMENT OF VARICOSE VEINS BY SICARD'S METHOD.

DRS. COVISA and SANZ DE GRADO.

As a result of the obliterating action of luargol and other arsphenamin preparations in intravenous injections in the treatment of syphilis, Sicard decided to apply this method to the treatment of varicose veins. As sodium is responsible for their thrombosing action, he employed for the intravenous treatment 10 per cent. sodium carbonate solutions in 10 to 20 c.c. injections. He treated in this way many patients in none of whom emboli occurred. He was able to cure varicose veins and ulcers with a few injections. The improvement was therefore immediate. Several patients had been treated in this way. Two of them were cured and the others remained under treatment with a favorable prognosis. Only local by-effects were noted when some drops entered perivenous tissue and necrotic foci were formed which remained a considerable time. Treatment was begun with doses of 2 and 3 c.c. of the 10 per cent. solution. More recently 5 c.c. were injected and the amount was increased 2 or 3 c.c. each time until 12 or 14 c.c. were reached. As a rule, the injections were given every other day or twice a week, but they could be applied every day without any discomfort when the varicose dilatations were numerous.

PRURIGO. DR. SAINZ DE AJA.

A 15-year-old girl, since she was 7 years old, had had pruriginous papular infiltrations which disappear spontaneously and reappeared leaving some discoloration. These lesions did not affect the flexor surfaces and showed a tendency to form groups; the masses were very small. The lesions were to be treated with pilocarpin.

VERRUCA PLANA JUVENILIS. DR. BARRIO DE MEDINA.

The patient, a girl, had had for several years a number of flat warts on the face and almost covering the dorsal surface of both hands. Dr. de Medina intended to treat her with neo-arsphenamin.

DR. COVISA said he did not believe neo-arsphenamin would cure the warts. He advised curettage, iodine, etc.

DR. BARRIO DE MEDINA said he was using this treatment only to confirm or deny the cures reported with arsenic.

SYPHILIS AND SUPRARENALS. DRS. BEJARANO and COVISA.

In textbooks there will be found descriptions of the late lesions caused by syphilis of the suprarenals, thus originating several well-known syndromes.

On the other hand, the functional changes caused by this infection in the suprarenals are usually overlooked. In our opinion, these changes should be blamed in the majority of cases for two symptoms often seen in syphilitic patients: asthenia and skin spots. For a long time it has been known that asthenia is a practically universal sign of syphilis which appears frequently toward the end of the secondary stage, either alone or accompanied by other secondary manifestations. It has been proved that asthenia is often accompanied by pigmentary changes. Most of these patients have, as has been observed, a lowered arterial tension, a fact of great importance when all these symptoms are traced to a decreased function of the suprarenals caused by the infection. This question is interesting not only theoretically but practically, since patients with pigmentary syphilis exhibit, as demonstrated by Ravaut, changes in the cerebrospinal fluid which are remarkable. It is probable that the same thing may happen in patients with asthenia, in which case the treatment should be intensified. These changes could be explained, as suggested by Baliña, by the close relation between the cortical substance of the suprarenals and the sympathetic nervous system and of the latter with the cerebrospinal nervous system. These conclusions may be made:

1. Syphilis often causes a change in the suprarenals, tending to reduce their activity.

2. Drs. Bejarano and Covisa believe that such symptoms as asthenia and pigmentation, frequently seen in syphilitic patients, may be attributed to this disease.

3. In these cases, besides vigorous specific treatment, the administration of epinephrin apparently is indicated, which at least in Baliña's cases, has given good results.

DR. BARRIO DE MEDINA, Secretary.

CHICAGO DERMATOLOGICAL SOCIETY

Regular Meeting, Feb. 16, 1921

CLARENCE A. BAER, M.D., *Presiding*

MUCOUS CYSTS. Presented by DR. STILLIANS.

The patient was a married woman, aged 30 years. Cysts had formed on the inside of the lower lip for several years, slowly becoming more frequent. The patient believed that grapefruit, eaten frequently, improved the condition. The cysts were painful, especially so just after they formed. She had had occasional attacks of mucous colitis and had peritoneal adhesions as the result of a laparotomy for abscess.

On the inner surface of the lower lip several mucous cysts could be seen, separated by macerated epithelium. The roof of one such cyst, examined microscopically, showed a horny thickening at the center.

DISCUSSION

DR. PUSEY thought the case was unusual and interesting on account of the history of the development of mucous cysts with acute inflammation of the lips. He could not see any cysts at this time, but the patient had an exfoliative inflammation of the mucous surfaces of the mouth.

DR. FOERSTER asked whether there had been any lesions on the palate at any time.

DR. SENEAR suggested the diagnosis of cheilitis glandularis apostematosa.

DR. STILLIANS considered the case interesting because he never had seen mucous cysts so small or multiple. It was impossible to get a probe in any distance, but there seemed to be a shallow depression forming the bottom of the cyst, and when the top of a cyst was placed on a slide he could determine thickening of the horny layer in the center of the lesion. The patient stated that she had noticed quite large, hard nodules on taking the tops of the cysts off, but was unable to get good ones for demonstration. Dr. Stillians was not sure whether the exfoliation was due to the cysts or to some applications of silver nitrate. No silver nitrate had been applied for a week, but the exfoliation appeared to be about the same. There was no oozing from the follicles at any time during examination, and the patient denied biting the lip. No lesions were present on the upper lip, but there were some on the cheek. The patient asserted that they were painful when they appeared, and she always opened them.

ACTINOMYCOSIS. Presented by DRs. ORMSBY and MITCHELL.

A farmer, aged 47 years, had had the disease for one year. The first change noted was neuralgia and soreness of the teeth on the left side of the upper maxilla. This was followed by swelling of the face in the contiguous area. At a later date, when the swelling became more pronounced, softening and rupture occurred, and more or less discharge had persisted since that time.

When the patient was first seen by Dr. Ormsby, in August, 1920, there was an egg-sized, boardy swelling, involving the entire thickness of the cheek and interfering with the movement of the jaw. Examination of the purulent discharge from a sinus revealed the ray fungus. During the six months' treatment some improvement had occurred through administration of arsenphenamin, potassium iodid and roentgen therapy, but the response to treatment in this case had been much less marked than in any of several others similarly treated.

A CASE FOR DIAGNOSIS. Presented by DR. STILLIANS.

A Canadian man, aged 25 years, had had attacks of itching dermatitis, beginning in the groin, for three years. The present attack had persisted since October, 1920.

At the time of presentation there was an eczematoïd dermatitis of the groins, the inner side of the thighs, the chest and abdomen. Beyond the border of the principal eruption were round, crusted, sharply defined macules, ranging in size to 1.5 cm., and a number of small pustules.

SEBORRHEIC DERMATITIS. Presented by DR. SENEAR.

A boy, aged 13 years, presented an eruption which began with a patch in the inguinal region, and then spread rapidly over the trunk, ten years ago. The disorder had cleared up somewhat at times, but had persisted to a considerable degree ever since. Itching was severe at the beginning of the trouble, but had become less intense; the patient stated, however, that the eruption "hurt." The boy also had a superimposed molluscum contagiosum two months ago.

DISCUSSION

DR. ORMSBY thought the diagnosis in the case shown by Dr. Stillians would lie between ringworm infection and seborrheic dermatitis, and believed ringworm could be ruled out on account of the rapid extension of the disorder over such an extensive surface. The amount of scaling and the crusting he considered typical of seborrheic dermatitis, and believed this diagnosis would stand first in this case.

The case shown by Dr. Senear he thought was similar, and he believed that seborrheic dermatitis and dermatitis herpetiformis would both have to be considered. The condition of the nails was probably onychia induced by pyogenic infection. There was much pus infection in the case, and the condition could be due to this. He did not feel positive about the diagnosis.

DR. STILLIANS said he had searched for fungi in his case but was unable to find any. There were pustules, in the border particularly, but he was most interested in the flat lesions with the sharply defined crusts.

DR. ORMSBY believed all the members were familiar with the clinical picture termed seborrheic dermatitis, particularly as seen behind the ears, on the neck and forehead, apparently induced by the micro-organism that induces ordinary impetigo. Whether true seborrheic dermatitis is caused by a single micro-organism is difficult to determine, but a clinical picture similar to it is not infrequently the result of different microorganisms.

DR. OLIVER stated that the boy had had several attacks of the same condition in the groin, and in childhood the face and scalp had been involved several times. He thought this would help to confirm the diagnosis of seborrheic dermatitis.

DR. SENEAR was of the opinion that Dr. Stillians' case was one of seborrheic dermatitis. Several months ago, when he first saw the boy whom he presented, the picture was somewhat different from that presented at this time. He then told the father that the diagnosis lay between seborrheic dermatitis and psoriasis, rather favoring psoriasis. The first attack cleared up rapidly under soothing treatment, with a little eruption persisting since then. At the time of the acute throat infection, about two weeks before presentation, there was an exacerbation of the disorder. Dermatitis herpetiformis had been suggested in the differential diagnosis not so much because of the clinical picture as on account of the statement of the boy that it hurt rather than itched.

There was multiformity and some pigmentation, some itching and a history of recurrence, but Dr. Senear was unable to make out any definite grouping in the eruption. He believed it was a case of seborrheic dermatitis, with the pustules present due to secondary infection, as Dr. Ormsby had suggested.

DR. BAER asked what Dr. Senear thought of the diagnosis of psoriasis for the nail condition, and wished to know how long it had been present.

DR. SENEAR, replying to Dr. Baer, said that psoriasis would be a strong possibility if he inclined to that diagnosis for the body, but thought it was not necessary to invoke a separate condition to explain the nail changes. That crusts, rather than scales, covered the body pointed more to seborrheic dermatitis than to psoriasis. The nails had been in the present condition for four or five years, possibly more.

SARCOID. Presented by DRs. ORMSBY and MITCHELL.

This patient was a woman who was first shown in January, 1919, and was presented at this time to show that the disease had progressed in spite of all

treatment. Histologic examination showed the deep type of sarcoid. Glandular involvement had recently developed underneath the chin, and nodules were present on the dorsal surface of both feet. She had received arsenic and arsphenamin, with little, if any, result.

MORPHEA. Presented by Drs. ORMSBY and MITCHELL.

The patient was a girl, aged 16 years, who presented lesions in a bandlike form extending over the upper two thirds of the forearm to the shoulder. The disorder was said to be of three months' duration. In the area on the forearm were several well-defined yellowish plaques varying in size from that of a five-cent piece to that of a silver quarter. Their peripheral zone was lilac tinted. On the arm the involved area was less indurated, showed none of the waxy plaques, and was hyperpigmented. Some paresthesia was present. The Wassermann reaction was negative.

In addition to the condition described, many atrophic white lines were present over both upper arms and in other situations on the cutaneous surface. The patient weighed 185 pounds.

DISCUSSION

Dr. ORMSBY stated that they had not studied the case particularly, and wished to know whether the gentlemen considered it an example of scleroderma or morphea. Clinically, there is much difference between the two disorders. These bandlike cases with light colored, ivory-like indurations surrounded with a purplish or violet border, he believed were morphea, and they are very different from scleroderma. The latter disorder begins with solid edema or atrophy and occupies a much larger surface. In his opinion this was a bandlike morphea.

Dr. PUSEY thought it was a case of morphea, and agreed that there is at least a clinical difference between morphea and diffuse scleroderma.

Dr. STILLIANS agreed with the diagnosis, and called attention to the fact that many of the patches ran together.

LICHEN PLANUS. Presented by Dr. STILLIANS.

An American woman, aged 53 years, had had an itching eruption since July, 1920. It began as water blisters over the whole body and had persisted as a dry rash since that time in spite of various methods of treatment. Itching was a prominent symptom.

There were widespread lesions of lichen planus with circinate lesions on the lumbar region, and on each shoulder was a patch of acuminate papules capped by horny scales.

DISCUSSION

Dr. STILLIANS stated that he had shown the patient on account of the patches of acuminate papules in a case of lichen planus.

LUPUS ERYTHEMATOSUS. Presented by Dr. WAUGH.

A man, aged 36 years, had had the disorder for three years. There was a reddened, scaling patch on the dorsal surface of each hand with considerable atrophic scarring. The areas involved had always been dry, and moderate itching and burning were present at times. The lower lip and lobes of the ears were moderately involved. A few lesions were present on the feet, similar to those on the hands.

DISCUSSION

DR. SENEAR said he saw this patient in August, 1918. At that time there was a generalized erythema of the face which would have been difficult to diagnose as a lupus erythematosus had it not been for the lesions on the hands and soles. The lesions at that time were bullous, and it had been suggested to the patient that the lesions had developed on a pernio basis. The eruption on the face seemed to begin after the patient was exposed to cold wind. He was at that time a driver on a coal wagon and might have been mildly frost bitten without realizing it. The disorder had cleared up readily, for lupus erythematosus, in three months, during which time he took quinin and used a calamin lotion and an iodine-benzol solution. As was to be expected, the result was not permanent.

DR. PUSEY thought the lesion on the left hand was certainly lupus erythematosus, but did not recall having seen lesions on the hand without any on the face in any previous case.

LICHEN SPINULOSUS AND SYMMETRICAL KERATODERMA. Presented by DR. SENEAR.

A married woman, aged 29 years, for the past three and a half years had had hyperkeratoses of the palms and soles. About four months before presentation she noticed that her entire body was covered with small elevations, like "goose flesh." There was no history of the administration of arsenic and no similar cases in the family. The basal metabolism rate was 104+.

DISCUSSION

DR. STILLIANS thought it was an interesting case, and expressed his pleasure at seeing the patient.

DR. PUSEY agreed with the diagnosis of an acquired hyperkeratosis.

DR. SENEAR said that in view of the interest in the endocrinous factors he had a basal metabolism test made in this case and received a report that it was 104+, and was told that this indicated no thyroid involvement.

TABES DORSALIS ASSOCIATED WITH SKIN LESIONS OF TERTIARY SYPHILIS. Presented by DR. BEESON.

A man, 57 years of age, gave a history of chancre twenty-two years ago. He did not notice any eruption or other trouble afterward. He took pills and a salty solution (probably potassium iodid) for about six months, and was then given permission to marry. About three years ago he began to have severe pains in his legs, beginning at the foot and shooting up to the trunk. About one year ago he began treatment for pulmonary tuberculosis under the care of Dr. O. W. McMichael. Steady improvement followed the use of tuberculin. The serpiginous syphilids appeared about six months ago, below the left scapula. They healed under specific medication.

Both knee jerks and Achilles' reflexes were absent and the patient was ataxic. There was no disturbance of urination, but bilateral Argyll Robertson pupils were present. An examination of the eyegrounds by Dr. Otto Wipper showed nothing abnormal. The vision was good. The blood gave a ++++ Wassermann reaction.

DISCUSSION

DR. PUSEY said that in his experience this was a rare combination. A number of years ago he had presented a similar case before the Chicago Neurological Society, and not one present at the meeting had seen the combination before.

DR. ORMSBY stated that a number of years ago there was a case at the Cook County Hospital in which tabes and the gummatous syphiloderm were simultaneously present. That was the only other case he remembered.

DR. PUSEY thought this was probably the same he showed to the Chicago Neurological Society.

DR. SENEAR thought this was an important point to establish since, in a paper just published by Dr. Wile, it was shown that skin lesions in connection with syphilis of the central nervous system were common rather than rare. If that is true, our teaching must be revised to cover this point. It was interesting to have an expression of opinion of the experience of others.

DR. MITCHELL said that there had been much discussion recently concerning the duality of syphilitic virus. Sicard contends that duality does not exist, whereas Marie and Levaditi insist that it does. The arguments have been gone into in extenso on both sides. It has long been observed that cutaneous lesions rarely occur in association with infection of the central nervous system. This is due, according to the duality theory, to the existence of two strains of spirochetes—a dermatropic and a neurotropic strain. The former, according to Milian, is an ulcerating strain, whereas the latter is a sclerosing strain. For this reason leukoplakia, which is a sclerotic process similar to the lesions of the central nervous system, is frequently observed in patients with syphilis of the central nervous system. Sicard contends that a neurotropic strain which does not produce cutaneous lesions would soon die out because of its inability to be transmitted from one person to another. Since the appearance of the articles by Sicard and others, a number of cases similar to the one shown have been reported in the French literature. Dr. Mitchell was interested in the subject, and desired to hear whether other members of the society had observed leukoplakias associated with tabes and paresis.

DR. FOERSTER said that Dr. Hirschl of the Krafft-Ebing clinic in Vienna maintained twenty years ago that neurosyphilis and syphilis of the skin do not occur together. Dr. Foerster recalled few instances of such association, although he had been on the watch for it during the past twenty years. Recently E. Hoffmann tried to show that the skin possesses a peculiar protective function for the internal organs in scarlet fever and other exanthems, as well as in syphilis, and that well-marked skin lesions in syphilis may indicate that the skin has exercised this function and served as a barrier to invasion of the central nervous system.

DR. MITCHELL called attention to the fact that Marie and Levaditi had found experimentally that the neurotropic strain in the rabbit would protect against the dermatropic but not vice versa. Others had not been able to prove this. Marie and Levaditi admit that this was not true in human syphilis.

DR. OLIVER said he had a patient under treatment who came to him with a marked leukoplakia, whose husband had advanced tabes. The woman had never had any symptoms of syphilis except the leukoplakia, which cleared up under antisyphilitic treatment.

DR. BEESON thought Fournier was the first to call attention to this combination, although Virchow had earlier performed a necropsy on a case of tabes with a muscle gumma.

In addition to the case mentioned by Dr. Pusey and Dr. Ormsby, Dr. Wile had shown a patient with gumma of the testes and tabes at the University of Michigan. Such cases seem relatively rare, but may be more common than is believed. He thought that probably some of them are not recognized. There have been about seventy-five cases reported, most of them in France.

DR. PUSEY did not accept the explanation that the reason tabes and syphilis were not seen together was because they were not recognized, for dermatologists recognize ordinary gummas on the skin, and certainly every dermatologist can recognize well developed tabes.

DR. FOERSTER said that he had seen abortive herpes zoster very early in tabes four or five times.

DR. BEESON said this patient had been treated for pulmonary tuberculosis for about a year and improved markedly on tuberculin. That condition appeared before the syphilitic lesions were seen, and the patient was referred to him from the clinic for tuberculosis.

DR. MITCHELL stated that Fournier thought that cephalic chancres were more likely to result in syphilis of the nervous system, but it has been convincingly demonstrated that there is no greater tendency in these cases toward syphilis of the nervous system than in others.

DYSTROPHY OF THE NAILS. Presented by DR. SENEAR.

A man, aged 28 years, whose disorder had been present for many years, had been treated in a number of dispensaries with various local measures, and had taken Fowler's solution without improvement. Repeated examinations for fungi had been negative, and there was no history of dermatoses.

Recently, on the advice of a relative, he had been taking a proprietary sarsaparilla tonic which contained potassium iodid, and improvement had been rapid. There was no history of syphilis, and the Wassermann reaction was negative.

DISCUSSION

DR. PUSEY asked whether Dr. Senear thought the therapy had helped or whether the condition improved spontaneously. He could record many failures under potassium iodid in such conditions of the nails.

DR. SENEAR said that the condition improved soon after the man began taking potassium iodid. He had received no drugs internally, except Fowler's solution. It might be a mere coincidence, but it seemed probable that the potassium iodid had affected the process in some way, although he did not know how.

ALOPECIA AREATA. Presented by DR. BEESON.

A boy, aged 14, with an extensive alopecia areata, also presented an ogilvate palate, two abnormally placed lower lateral incisors, which were posterior to the other teeth. He was microcephalic and subnormal mentally, but no characteristic evidence of syphilis could be discovered. The Wassermann reaction was negative.

DISCUSSION

DR. MITCHELL said that Leredde had recently contended that itching dermatoses, particularly lichen chronica simplex, were of syphilitic origin, and it

was interesting that this patient who had microcephaly, a highly arched palate, alopecia areata and marked dental deformities had also lichen chronica simplex on the nucha, which in his experience was rare in that location in the male.

DR. BAER said, as he recalled it many years ago as a student in Paris, most of the cases had lichen chronica simplex.

DR. PUSEY asked whether any one had thought there was any evidence that the boy's congenital defects were syphilitic. He could see none.

DR. BEESON replied that he had been unable to discover any syphilitic history.

PARAPSORIASIS. Presented by DR. STILLIANS.

A married woman, aged 28 years, had been well until the summer of 1917, when she developed a genital sore. One month later red spots appeared on her neck; these gradually faded away, but reappeared on the arms and chest, where they had persisted since that time, with varying severity. The patient stated that the condition improved on tanning, and following an attack of furunculosis.

Examination revealed many pale pink to red macules covered by a wrinkled, horny layer or by frank scales. Some, denuded of scales, were bright red with a thin, epidermal layer. The patient had received arsenic internally and hypodermically without effect.

DISCUSSION

DR. PUSEY thought it was a case of guttate parapsoriasis.

DR. FOERSTER had presented a patient before this Society with the same type of lesions about three or four years ago. The man recovered completely during service at the front in Italy, without medication, and ascribed his relief to frequent bathing in the rivers and lakes. Dr. Foerster called attention to reports from Vienna where they had recently been giving from twenty to thirty injections of pilocarpin to patients with parapsoriasis with satisfactory results.

DR. STILLIANS agreed with the diagnosis of parapsoriasis, but said the patient had been bothered a good deal on account of a diagnosis of syphilis.

CHICAGO DERMATOLOGICAL SOCIETY

Regular Meeting, March 15, 1921

ARTHUR W. STILLIANS, M.D., *President*

A CASE FOR DIAGNOSIS. Presented by DR. STILLIANS.

An American woman, aged 49 years, complained that her tongue felt as though it had been scraped. This sensation was first noticed late in December, 1920, and was present at first in the left side only, but for the past several weeks had been present in the right side also. Red spots, which lasted for only a few hours, appeared and reappeared on the inside of the cheeks, and were accompanied by a feeling of heat. The pain in the tongue was almost constant, and at times shooting pains were added; the discomfort was not increased by eating, and was said to be decreased slightly by talking.

An alveolar abscess was cleaned up seven weeks ago, several bad teeth were removed and a tonsillectomy was performed four weeks ago. The red blood count was 3,160,000; hemoglobin, 55 per cent.; color index, 86; poikilocytosis, marked; white blood count, 13,700, with an increase of neutrophils. Marked intestinal intoxication was present. On the right border of the tip and at the posterior part of the left border pronounced reddening of the tongue could be seen, and there were a number of red macules, not sharply defined, on the inside of the cheeks, lower lip and anterior pillar of the fauces.

DISCUSSION

DR. PUSEY said that he saw on the buccal mucous membrane little areas of erythema; not definite patches, but long, crescentic lesions. The patient did not have Moeller's glossitis. She might have subsiding lesions or erythema multiforme, but one must always suspect pemphigus when he finds lesions like these in the mouth that cannot be explained. He thought there were inconsistencies about the case, and did not understand how any of the spots he saw could be painful.

DR. LIEBERTHAL asked how long the condition had been present and whether there had been any free intervals. He thought there was no evidence of pemphigus and suggested herpes as a diagnosis.

DR. STILLIANS, replying to Dr. Lieberthal, said the trouble had been present since Christmas, and there had been no free intervals. The patient complained a good deal of spontaneous pain, which was relieved by talking. He did not think the case was sufficiently severe to diagnose as Moeller's glossitis, and the lesions were not typical of that disorder. The patient had stated that she never had any tags of epithelium around the red spots, and that the tongue was painful before any red spots developed. The etiology was supposed to be the alveolar abscess which had occurred several weeks before the onset of pain in the tongue.

DR. SENEAR did not think that the condition was Moeller's glossitis. He thought the lesions were all located on the tongue and mucous membrane in locations in which the tissues might have been bitten, and since the patient, said to be neurotic, stated that the pain preceded the lesions, he thought it possible that the entire process might be traumatic.

DR. BEESON thought the condition was traumatic or gastro-intestinal.

DR. McEWEN said he had always been impressed with the fact that certain tongue conditions, which seem to be permanently painful, show little evidence of abnormality as far as appearances go. He believed that if the patient were biting her lips or tongue there would be more visible evidence of traumatization.

DR. PUSEY was inclined to believe that the exfoliation in the mouth was associated with gastro-intestinal disturbance. He was impressed with Dr. Lieberthal's idea. It was not a frank aphthous stomatitis, but possibly an abortive herpes that did not become well developed vesicles. He did not think the lesions were traumatic because they were present in spots in which the patient could not produce them by biting.

A CASE FOR DIAGNOSIS. Presented by DR. STILLIANS.

An American girl, aged 8 years, in the spring of 1916 had had sore throat and fever for one day, and a few days later her hair began falling. Since that time she had had lobar pneumonia and bronchopneumonia, and the hair

had fallen after each illness. It had fallen at other times when exposed only to chilling of the head or when the head perspired, which it frequently did, and the hair recently fell out following a severe coryza.

The blood count was practically normal; the urine contained indican, and albumin was present for a time during the coryza. Basal metabolism was reported — 6.

A fringe of hair about 2 inches long was present about the border of the scalp; the rest of the scalp was covered by very short new hair. Specimens of the recently lost hairs showed swelling in the upper follicular portion.

DISCUSSION

DR. OLIVER thought it might be a case of alopecia areata that did not involve the eyebrows and lashes.

DR. LIEBERTHAL thought it was a recurrent toxic alopecia, as the growth of the hair was not interrupted. He suggested putting the child on thyroid extract.

DR. PUSEY thought alopecia areata could be ruled out. The alopecia was not in patches, but left a regular fringe about the border of the scalp. It was not alopecia totalis, nor a diffuse alopecia because the diffuse alopecias are universal in the areas involved. He agreed with Dr. Lieberthal that it was an extraordinary example of toxic alopecia. He did not see evidence of the endocrin disturbance, but believed the child's hair was extremely sensitive to toxic conditions. In his opinion, it was a case of ordinary toxic alopecia greatly exaggerated.

DR. STILLIANS said that the hairs he examined were swollen in the upper follicular portion tapering to normal size above and to a point below. There was no abnormality of the skin. He could not account for the eyebrows and lashes not being involved. He had thought of alopecia areata on account of the long tag that had grown out on one side when the patient was first seen, but now considered that diagnosis almost impossible, and agreed with Dr. Lieberthal's diagnosis of toxic alopecia. The patient had improved, but her hair had never been normal since the age of 4 years.

LYMPHANGIOMA. Presented by DR. STILLIANS.

An American woman, aged 56 years, presented a skin deformity which had been present for more than ten years, but which was not present during girlhood. In front of the right ear there was a soft, flat-topped bulla which was yellowish under the diascopé, brown at other times; it was oval, 1.5 by 1 cm. in size. No subjective symptoms were present.

DISCUSSION

DR. PUSEY thought the growth was a soft, jelly-like epithelioma, and believed it should be scraped off and examined. As to treatment, the base could be cauterized with zinc chlorid and radium applied. He thought this would be the last of the growth.

DR. McEWEN was reminded of a patient whom he had shown the Society several years ago with a similar lesion on the bridge of the nose. Roentgen therapy was used unsuccessfully and radium was tried, with partial success, after which the patient passed into other hands. He had seen him recently and found that he had been treated with radium extensively; the lesion was still showing some activity.

DR. LIEBERTHAL asked why carbon dioxid snow could not be used successfully.

DR. PUSEY said carbon dioxid snow should not be used in carcinoma, as it is not sufficiently destructive.

DR. STILLIANS said he had not thought of an epithelioma but now realized that the lesion was much too dark for a lymphangioma; he would investigate the case further.

LUPUS ERYTHEMATOSUS. Presented by DR. STILLIANS.

An American woman, aged 43 years, presented an eruption which had been present on her face for two years and on her back for one year. Radiotherapy had failed to give relief, and she had afterward been treated with caustic paste at a sanatorium in Missouri.

On each cheek was a large, dense, bright red scar within and beyond which there were a few recurrent lesions of lupus erythematosus. There were no signs of tuberculous lesions elsewhere, except a relative lymphocytosis and leukopenia. The small lesion on the back had been excised for study.

DISCUSSION

DR. McEWEN asked what treatment the patient had received and whether the scars were supposed to be due to the treatment.

DR. STILLIANS stated that someone had used a caustic paste on the lesions, causing great pain with prompt recurrence of the lesions as soon as the parts healed.

DR. PUSEY said he had seen much greater scarring from the excessive use of carbon dioxid snow.

DERMATITIS NODULARIS NECROTICA. Presented by DR. STILLIANS and DR. OLIVER.

The patient was a white man, aged 43 years, a laborer by occupation. He was first admitted to the Cook County Hospital in June, 1919, at which time the skin eruption had been present for seven years. The lesions began on his legs, later becoming generalized so that at the time of admission they were present on the head, trunk, back and extremities. They varied in size from that of a pea to that of a quarter, a few being even larger. They were discrete, oval or circular in shape, and some of the older ones were covered with fine scales. New lesions were indurated, copper colored papules which itched when they first came out; the centers gradually became necrotic and an ulcer formed covered with a thick black crust. On healing thin scars remained.

When the patient was first admitted, he was highly toxic and suffered from marked systemic symptoms. One notation on his chart, made June 17, 1919, stated: "Patient's mind seems cloudy; temperature 103 F.; pulse good; dyspneic but no lung findings. Condition is serious."

Culture from the pus under the crusts showed a pure staphylococcus growth. A vaccine was made and administered subcutaneously. The Wassermann reaction was negative; white blood count 8,000; the urine was negative. The patient gradually improved and was discharged, July 26, 1919.

On March 1, 1921, he returned to the Cook County Hospital with a recurrence which was not nearly so severe as the former attack. The lesions were of the same type, and the scars from the previous attack were present, par-

ticularly on the lower limbs. Cultures again showed staphylococcus albus; the temperature was normal; the white blood count was 9,700—60 per cent. lymphocytes. Physical examination and a roentgenogram of the lungs were negative. The diagnosis of dermatitis papillaris necrotica had been made by the late Dr. Frederick Harris.

DISCUSSION

DR. SENEAR thought the diagnosis of dermatitis nodularis necrotica was proper by exclusion, although he had never seen a case of this disease before. He thought it did not belong to the leukemias, as there would probably have been more change in the general condition during the years which the disorder had been present.

DR. ZEISLER thought it was a nodular dermatitis with necrosis, and considered it one of the most extraordinary cases he had seen. The report of two cases had been published in the *Iconographia Dermatologica*, one of them in a child with lesions on the buttocks, which he thought no one would hesitate to call a papulonecrotic tuberculid. The other patient had necrotic lesions on the legs, and foci of tuberculosis were demonstrated in the lungs. Dr. Zeisler had thought of some of the leukemias or pseudoleukemias in connection with the present case, and believed this man might develop such a disorder.

DR. MCEWEN thought the credit for the diagnosis in this case belonged to the late Dr. Harris, who had charge of the man during his first stay in the hospital. At that time the patient was in a bad condition from drink, exposure and filth, and it was believed at first that the lesions were the result of these factors. It was considered one of the most remarkable cases ever seen in the Cook County Hospital.

DR. LIEBERTHAL believed the possibility of tuberculosis should not be left out of consideration. The lesions on the hands looked much like a papulonecrotic tuberculid, and the vaccination-like scars would also suggest this disease. He hoped Dr. Stillians would report the microscopic findings.

DR. PUSEY said the case was practically a replica, although more intense, of a case of dermatitis nodularis necrotica in a patient that Dr. Harris had treated several years ago. That patient was a well-to-do man who was heavy and rather flabby, in whom they tried to find some constitutional disturbance or focus of infection to account for his trouble, but as far as Dr. Pusey remembered nothing could be found. He thought the condition might be a papulonecrotic tuberculid, but that it was not necessary that it should be. Sometimes dermatitis nodularis necrotica itches a great deal, and this is not a characteristic of the tuberculids. Dr. Pusey had seen a papulonecrotic tuberculid that approximated in extent this man's case, in a boy of 15 or 16 who was developed like a boy of 12. In this case there was no disturbance of sensation, and the condition was accompanied by Sternberg's tuberculosis. The condition of the legs was probably due to stasis. He had thought of vagabondism, but that would not account for the lesions on the body.

A CASE FOR DIAGNOSIS. Presented by DR. STILLIANS and DR. OLIVER.

A man, aged 42 years, a laborer, presented a cutaneous disorder which had been present for ten months. There was no history of a previous attack. The onset followed a series of twenty hypodermic injections of unknown nature. The first Wassermann reaction was reported as anticomplementary.

The skin of the trunk and extremities was very dry and separating in large scales. There was no redness or other sign of inflammation.

DISCUSSION

DR. PUSEY considered it a case of xeroderma. The history in such a patient was not of much weight. The man had probably taken so few baths before he had received the injections that he had never noticed the disorder.

DR. McEWEN asked whether any one had observed untoward skin disturbance from sodium cacodylate.

DR. PUSEY said he had seen sodium cacodylate produce generalized exfoliative dermatitis. He had a patient with psoriasis who was given sodium cacodylate at a sanatorium for supposed syphilis until he developed a universal exfoliative dermatitis. The eruption was universal, and the palmar lesions were characteristic of arsenic. The patient was improved greatly by keeping him oiled and at rest, and Dr. Pusey had learned since that he was well except for the palmar lesions.

DR. STILLIANS said this man insisted that his skin was all right before he received the injections, and that this condition developed only after treatment.

MYCOSIS FUNGOIDES. Presented by DR. ZEISLER.

A woman, aged 32 years, had been under observation for five years, the disorder having first appeared eight years ago. There were recurring lesions in the axillary and popliteal spaces and in the groins. The lesions had cleared up rapidly under arsenic and radiotherapy. The lesions at first were moist and eczematous, but under the influence of roentgen therapy they dried and cleared up. She had been free from lesions at various times in the past five years. Itching was present. (This case was reported in full by Dr. Joseph Zeisler in the *Medical Clinics* of Chicago, 1916.)

DISCUSSION

DR. ZEISLER said it was a case of mycosis fungoides. The patient had had tumor formation at times, but this had rapidly receded under roentgen-ray treatment and arsenic taken internally. Large gyrate lesions of mycosis fungoides had been present at various times during the past five years, and the patient returned every year or so for treatment.

DR. LIEBERTHAL thought it was a wonderful result from treatment for there was no vestige of the former condition present at this time.

DR. SENEAR agreed with Dr. Zeisler's diagnosis, and called attention to the fact that extreme undermining was taking place at the edge of the lesion.

A CASE FOR DIAGNOSIS. Presented by DR. EISENSTAEDT.

A woman, aged 27 years, presented a lesion on the chin which had been present for two years. She had been treated at a homeopathic clinic. During the last eight months the lesion had acquired a zone of redness. The patient had first been seen by Dr. Eisenstaedt one week previously. The lesion had been lanced twice at Ann Arbor Mich., and only blood had been obtained.

DISCUSSION

DR. PUSEY thought from the acuminate character of the lesion it was a cyst of some sort. It had about the consistency of a mass of tuberculosis, but

he did not believe one would get the conical, pointed lesion from that disorder. He thought it persisted because it was a cyst, and puncturing did not destroy the sack.

DR. MITCHELL thought it was a cyst.

DR. SENEAR believed it was a cyst, but thought on account of the purplish color one should keep in mind a melanoma, although the shape of the lesion did not suggest this.

DR. BEESON believed it was a cyst.

DR. EISENSTAEDT was impressed by the peculiar color which Dr. Senear noticed, and the idea of a possible lymphangioma or a melanoma occurred to him. He had first seen the patient one week previously, and she stated that the lesion had persisted for two years and that only blood came out when it was punctured. The idea of a cyst had not occurred to him, but he saw the possibility of its being such a growth.

DR. PUSEY thought an accumulation of blood might account for the black spot in the center of the lesion. He suggested that it be opened, the contents scraped out and the actual cautery applied to the wall. He believed this would eradicate it and not leave much of a scar.

DR. SENEAR said he had seen a patient with a lesion similar to this, a deep-seated lesion with much the same color. Proceeding on the theory that it was a cyst, Dr. Pusey had punctured it with the actual cautery. Only blood was obtained, and the lesion disappeared temporarily but recurred; on repuncturing, it again disappeared. That lesion was in the cheek and on opening the mouth to get the finger in he found definite varices of the veins of the mucous membranes and believed the lesion in the cheek was a varicositis. The cautery was used because they feared a malignant growth.

DR. STILLIANS said Dr. Eisenstaedt had suggested that it was an atypical angioma, a variation of the spider nevus with a small cavernous lesion in the center. He thought this was plausible, and that it might account for the lesion.

ANGIOKERATOMA OF THE TOES. CHILBLAIN CIRCULATION OF HANDS. Presented by Drs. PUSEY and SENEAR.

A young woman, aged 29 years, who had been shown in 1917, with angiokeratoma of the toes and fingers, showed a severe chilblain circulation in the hands, the latter being puffy and bluish in color. The lesions had been destroyed by fulguration and electric cautery, and there had been only few recurrences. The patient was shown at this time because she had begun to develop punctate angiomas of the mucous membranes.

DISCUSSION

DR. EISENSTAEDT said it was a typical case of angiokeratoma, and the extraordinary chilblain circulation of the hands was either stationary or getting worse. He thought it would be interesting to try to accomplish something therapeutically, but he knew of nothing to do for chilblain circulation in the hands. At present, he was taking care of a strong, robust man who had a similar condition of the feet. There was a peculiar disturbance of circulation, with three distinct ulcers, the first one of which appeared three months ago. He had succeeded in almost entirely healing the ulcers, but beyond that point he was at a loss to know what to do. He had used galvanism, which was

purely palliative. Just what similarity there was between these cases and a definite gangrene seen in a young man of 26 years recently, he did not know. He had used Ringer's solution for that condition, but this type of a case he considered different.

DR. PUSEY thought the case was interesting in the results of treatment. He did not understand how any one could consider the condition an angiokeratoma, for no keratomas were left. Dr. Senear had removed them by means of fulguration and the cautery. As to the asphyxia in the extremities, it was progressing, and he believed this was a fundamental disturbance that could not be corrected.

DR. SENEAR thought the development of lesions in the mucous membrane during the last six months was interesting. In view of the mucous membrane lesions, he was inclined to look on the development of the lesions on the hands and feet as entirely independent of chilblain circulation, although the latter had perhaps increased the severity of the condition. There were no active mucous membrane lesions at this time; they had evidently become thrombosed and disappeared spontaneously, but a week ago the patient had one definite new lesion and one involuting lesion.

VERRUCOUS NEVUS. Presented by DR. MITCHELL.

A boy, aged 9 years, presented a verrucous hairy lesion on the left buttock which had been present for five years. The father was not absolutely certain about the duration, but felt sure that the lesion was not present at birth.

The lesion was a semicircular, verrucous lesion with numerous coarse hairs, and comedo-like lesions about either end. Various methods of treatment had been tried before the patient came under observation.

DISCUSSION

DR. ZEISLER considered the lesion a tuberculosis verrucosa cutis.

DR. EISENSTAEDT agreed with Dr. Zeisler.

DR. PUSEY said he could not, on account of the abnormal growth of hair, see how it could be a tuberculosis verrucosa cutis, but it might well be a verrucous nevus.

DR. SENEAR thought the scarring pointed to a diagnosis of tuberculosis verrucosa cutis.

DR. MITCHELL believed it was a verrucous nevus which had been treated with carbon dioxid snow. The father said it was not present at birth, but he was not quite sure about it on close questioning. No biopsy had been obtained, but considering the hair and other symptoms, he thought the diagnosis of verrucous nevus was correct.

LESION ON THE TONGUE. Presented by DRS. ORMSBY and MITCHELL.

A man had received treatment at the Central Free Dispensary since October, 1918. At that time he had a primary lesion and was given injections of arsphenamin but no mercury, as he could not tolerate this drug. He had a lesion on the forehead and others which he described as felons. He was first seen by Dr. Mitchell two days ago, after having received six intravenous injections within a few weeks. Lesions had recurred on the

tongue, and the one now present had resisted all treatment. At the time of presentation the Wassermann reaction was negative.

DISCUSSION

DR. PUSEY thought the lesions were recurrent syphilis.

DR. ZEISLER thought it was tuberculosis of the tongue. Jadassohn had described a chancriform type of tuberculosis of the tongue characterized by its chronicity and resemblance to chancre and epithelioma. In his opinion, the lack of response to antisyphilitic treatment would rule out syphilis.

DR. MITCHELL said that the condition had resisted all previous treatment. He had seen the patient in the Dispensary and considered the patient interesting as one of those who will sometimes float along, come in and have an injection and receive it without any questions being asked. The Wassermann reaction was negative at present, and had been since early in the course of the treatment. He had first seen the patient only a few days previously.

DR. LIEBERTHAL thought it was not surprising to see patients of this kind. He had recently seen a patient who had received thirty injections of arsphenamin at a clinic. He had had a glossitis in the beginning and after three injections the condition cleared up, but two or three weeks later the tongue was again sore. The patient ultimately came to Dr. Lieberthal, and as he had received enough arsphenamin he put him on mercury, as he also had a palmar syphilid which was not clearing up. The patient was given injections of calomel, and then said he could not stand the injections on account of the pain, so salicylate was substituted. The man had now been free from symptoms for some months without the administration of arsphenamin. Dr. Lieberthal thought one should be exceedingly careful about employing arsphenamin after it had been used over a long period. He intended to subject his patient to further intensive mercurial treatment.

DR. MITCHELL said that, according to this man's story and history, he could not tolerate mercury.

DR. OLIVER stated that he had seen this patient once at the night clinic at the dispensary, and at that time the lesion looked like a recurring syphilitic lesion, although tonight there seemed to be more induration.

LICHEN PLANUS. Presented by DR. JACOBSON (by invitation).

A negro, aged 24 years, presented an eruption which had been present for two months and was accompanied with considerable itching. The eruption was first noticed on the flexor surfaces, gradually becoming generalized. At the time of presentation the Wassermann reaction was negative. Thickly set on the forearms, more discretely on the arms, shoulders, neck and thighs, were circinate lesions consisting of a dark brown, macular center surrounded by an elevated ridge 1 or 2 mm. wide and 1 mm. high, which was about the color of the normal skin (light brown). These lesions were confluent in places on the forearms, presenting a striking appearance. Here and there in the vicinity of the circinate lesions could be seen flat, angular papules. No lesions were found in the mouth and a few about the genitalia.

DISCUSSION

DR. PUSEY thought the case was an extensive one of lichen planus in the negro, and that it was an interesting and beautiful example of that disorder.

SCARS FOLLOWING ZOSTER OF THE NOSE. Presented by DR. STILLIANS.

A man aged 35 years, stated that several months ago he had had a peculiar sensation along the left side of his nose, but no pain. Following that two crusted spots appeared, one on the left side of the tip of his nose and one on the left side of the bridge, and persisted for several weeks. When the crusts were removed deep ulcers remained, but finally healed. The left side of the nose was numb for some time, but there was no pain at any time.

Near the tip of the nose on the left side was a depressed scar 0.7 cm. in diameter, with dilated blood vessels crossing it. On the left side of the bridge of the nose was situated a depressed scar 0.3 cm. in diameter, covered by skin of nearly normal color and texture. All blood examinations were reported negative.

DISCUSSION

DR. OLIVER pointed out that there was definite telangiectasia around the edges and in the center of the spot, and believed epithelioma should be considered.

DR. SENEAR thought the lesion was only a scar made up of two parts—a large depressed, irregularly outlined scar with a tumor formation, traversed by well defined telangiectasia at the center. He believed the picture might be produced by a keloid formation at the center of a scar.

DR. STILLIANS said he had considered zoster, but the patient said there had been no pain. He had thought of an epithelioma on account of the shape and the fact that the center was soft.

JAMES HERBERT MITCHELL, Secretary.

NEW YORK DERMATOLOGICAL SOCIETY

Regular Meeting, Feb. 22, 1921

JAMES MCF. WINFIELD, M.D., *President*

CASE FOR DIAGNOSIS. Presented by DR. TRIMBLE.

The patient was a young man, aged 26, born in Canada. His previous history was of no consequence, except that he had had infantile paralysis when a child, which had permanently affected the left arm.

His arms and forearms from the shoulders to the wrist were thickly studded with great numbers of small guttate lesions, rather uniform in size; slightly infiltrated, and mildly pink with a marked yellow hue. Some of the lesions were distinctly infiltrated, giving a papular feel to the finger. The lesions itched slightly, but the pruritus was not a marked factor.

The eruption was also present on the chin and sides of the mouth, and resembled a superficial seborrheic eczema in these locations. The duration was one year, the eruption having begun on the neck and spread downward. There was no venereal history, and the Wassermann test was negative.

DISCUSSION

DR. KINGSBURY suggested that there might be an element of xanthoma in the condition, notwithstanding the scaling. The way the striae ran on his arms,

beginning on the neck, suggested some metabolic disturbance. The patient was evidently not in good health, and the urinalysis might reveal glucose; or the blood chemistry might show an abnormal condition.

DR. WILLIAMS said that if the condition had been in a child instead of a man of 20 odd years, he might have thought it a case of urticaria pigmentosa. As it was, he did not know what to think of it.

DR. WISE thought it might be a form of parapsoriasis. It did not seem to be a xanthoma, as it was not yellow enough, nor was there enough pigment to suggest urticaria pigmentosa. A biopsy would probably reveal the diagnosis.

DR. LANE said that he felt it was impossible to make a diagnosis of this case at present without a biopsy. He had never seen a case of parapsoriasis with as much thickening of the patches and elevation of the lesions as was present in this case. The lesions themselves and their distribution bore more resemblance to urticaria pigmentosa.

DR. HIGHMAN did not think anything definite could be said about the case. The first diagnosis that occurred to him, and the one he most leaned to, was urticaria pigmentosa, since the lesions resembled that condition more than any other. The striping was significant, and both the distribution and arrangement were seen in children with urticaria pigmentosa. The fact that the condition occurred in adult life was rather against that diagnosis, but no other clinical entity seemed to conform to the picture the patient presented.

DR. TRIMBLE said he had seen the patient only once, the previous afternoon, and on examining him carefully several diseases were thought of as a diagnosis of the condition, only to be discarded. Parapsoriasis guttata received most consideration, although the nodular character of the lesions was against that diagnosis. Tinea versicolor was considered but could not be proved. Xanthoma had occurred to him, though it seemed like a stretch of the imagination to consider that condition. Urticaria pigmentosa had not been considered. The patient's lesions might possibly be a type of lesion he had seen on two previous occasions—xanthoma elasticum. One of the patients he recalled vividly; the lesions appeared on the side of the neck and resembled this eruption somewhat. The eruption had a definite linear arrangement, and was the same color as the lesions on the patient shown. There was a tendency to form lines in the elbow flexures of the present patient.

The patient's scalp had been examined carefully, for it was thought the condition might be a seborrheic eczema, but that diagnosis was also discarded. The man's general health seemed to be below par. A blood picture might help clear up the diagnosis.

CASE FOR DIAGNOSIS (PROBABLY PARAPSORIASIS). Presented by DR. TRIMBLE.

A man, aged 39, a native of the United States; presented irregular, pinkish noninfiltrated patches, mainly on the trunk; they ranged in size from that of a ten-cent piece to that of a silver half dollar, and there was practically no scaling. Mild itching was a feature, and the duration of the condition was six months. The tentative diagnosis was parapsoriasis of the type érythrodermie pityriasque en plaque disséminées.

DISCUSSION

DR. WISE agreed that it was difficult to determine the difference between a parapsoriasis and a premycotic erythema in many instances. He thought this case was one of parapsoriasis.

DR. CLARK said he had seen no infiltration in the lesions, and there was not the itching usually present in a premycotic erythema. He thought the condition was parapsoriasis.

DR. HIGHMAN was strongly inclined to believe that it was a premycotic eruption. The condition was rather more glazed and edematous than one would expect in parapsoriasis, and the situation of the erythema on the lower half of the body was in favor of early mycosis.

DR. WILLIAMS thought it a premycotic erythema. There was little scaling and a distinct infiltration of some of the lesions and a slight swelling, particularly in the lesions over the left iliac crest—about what one would expect in the earlier stages of a premycotic erythema. Dr. Highman had spoken of the glazed appearance which is characteristic; in parapsoriasis one would expect, not a smooth surface, but a rough or slightly scaly surface. The fading out of the periphery was more like a premycotic condition than a parapsoriasis. Probably, if the man were watched long enough, he would develop a mycosis fungoides.

DR. SCHWARTZ thought the condition was parapsoriasis.

DR. G. H. FOX said he had seen a number of cases which turned out to be typical mycosis fungoides in which the patient at the outset presented the same eruption that this man had.

DR. WINFIELD said he could find no one lesion that was scaly, and the one on the arm inclined him to agree with the diagnosis of premycosis.

DR. LANE said that Dr. Clark had remarked on the lack of induration or infiltration in a premycotic erythema. It was his impression that in premycotic erythema there might be no palpable infiltration for a considerable length of time.

DR. CLARK replied that that might be correct, for there must be a stage in which there was no infiltration in the lesions. None of these showed any infiltration.

DR. WISE referred to a case presented by Dr. Pollitzer about fourteen years ago as a possible case of premycosis. The patient was a New Jersey physician whose body was covered with infiltrated scaly lesions; the biopsy revealed changes which were interpreted to be parapsoriasis. The patient was still living and actively engaged in practice; the eruption had persisted, but showed no evidence of fungoid lesions.

DR. G. H. FOX said that while pruritus was often intense in the early stage of mycosis fungoides, there were cases in which it was notably absent, especially when there were erythematous patches such as this man had.

DR. TRIMBLE said that he had thought of several of the diagnoses discussed before presenting the case. At times when the diagnosis of parapsoriasis is made it turns out to be premycosis, and vice versa. His own inclination in this case was to parapsoriasis, for the reasons presented by several of the members.

PEMPHIGUS OF THE MOUTH. Presented by DR. CLARK.

Mrs. M. S., aged 43, born in the United States, married, the mother of one child, was in good health. The patient was never vigorous, but her general health had always been good, and she was always able to do everything; she had had all the children's diseases except whooping cough. Her last serious illness was at 11 years of age. She was operated on nine years ago for a prolapse of the stomach, and six years ago had a tumor, probably ovarian, removed from the right side.

Seven or eight years ago she noticed that the gums of the lower jaw were receding and that they had become spongy. She was then wearing a plate in the upper jaw and was frequently troubled with canker sores under the plate; she had a new plate adjusted, and all teeth were cleaned and treated. About four years ago all teeth were extracted as the whole mouth was then sore, especially the mucous membrane of the cheeks. Since that time, at intervals, the roof of the mouth and the mucous membrane of both cheeks had been sore. From time to time the edge of the tongue had been tender and sore.

As presented, the patient had no teeth. The gums were retracted, healed and apparently normal. The roof of the mouth showed no lesions. On the buccal mucous membrane on both sides were seen areas with superficial slough and several beef-red, raw, level areas, previously the site of blisters or bullae. The left side of tongue near the tip showed an irregular slough, as if it had been touched with silver nitrate.

The patient's general health and the condition of her mouth had improved considerably during the past six months under big doses of arsenic, but the condition of the mouth had never healed. Due care and consideration had been given to the patient's digestive apparatus, and she had been almost entirely on a vegetable diet. She seemed to be well nourished (weight, 130 pounds), with a good color and complained only of the extreme soreness in her mouth.

The blood and spinal fluid were negative to the Wassermann and other tests, and smears and cultures from the mouth failed to show anything unusual.

DISCUSSION

Dr. HIGHMAN agreed with Dr. Clark's conception that the condition was pemphigus of the mouth, in spite of the fact that it had remained so long without any outbreak on the body; for in the vast amount of material seen at Mount Sinai Hospital there were cases of buccal involvement that had lasted as long as two to five years preceding cutaneous involvement. When it appears the patients usually succumb rapidly.

Dr. TRIMBLE commented on the increasing frequency of these cases within the last year or two. He had seen a patient with Dr. Bechet a few weeks ago who had gone on without any cutaneous appearance or outbreak. Another patient had come to the office three days previously; the last one he had seen had had lesions in the mouth for eighteen months before there were any lesions on the body. He was beginning to think that whenever distinct blebs appear and continue to recur in the mouth, regardless of their size, they nearly always turn out to be pemphigus lesions.

Dr. BECHET said he thought that in these cases of bullous eruptions in the mouth, the diagnosis of pemphigus should be entertained, especially if other diseases could be excluded. Treatment undertaken early might possibly check further development of the disease. This had been especially brought to his

attention by the observation of two recent cases. Both patients had developed a fulminant pemphigus eruption on the body, after it had remained localized in the mouth for months. One of the patients had had lesions in the mouth for a year before they appeared on the body. Three months after their development she was moribund. In the other case the oral lesions had been present for three months—the body was entirely free. She was presented at the New York Academy of Medicine on Jan. 4, 1921, with a tentative diagnosis of pemphigus, which was not agreed with, the consensus of opinion being that it was an aphthous stomatitis. One month later an extensive bullous eruption, typically pemphigoid in character, developed. The diagnosis was unquestioned by this society. Six weeks after the appearance of the eruption there was a marked asthenia, and an approaching fatal termination was plainly evident. These two cases might possibly have followed a more favorable course if they had been recognized earlier.

DR. WINFIELD said that this case of Dr. Clark's was almost a counterpart of one that he himself had reported at a previous meeting.

DR. CLARK said he had put a question mark after the diagnosis because of the positive history of a generalized bullous eruption in the mouth for a period of five years without any eruption on the body, and probably a history of an eruption extending over a part of the mouth for two years before that. The patient had gained distinctly after the administration of big doses of Pearson's solution in 15 minim doses, taken in milk of magnesia during the day, while on a vegetable diet. She tolerated arsenic very well, and had been taking it off and on for the past year.

He had hoped there would be some discussion as to what more might be done for her to prevent an outbreak on the body. Pearson's solution was the sodium salt. She had been taking about seven doses a day, at two hour intervals.

DR. HIGHMAN mentioned three other methods of treating pemphigus that were useless—with arsphenamin, silver arsphenamin and Coley's fluid. After one injection of the last a patient seemed better, but later became worse. It did not seem reasonable to put a patient of this kind on a vegetable diet. The condition was plainly catabolic, and the patient should be nourished as much as possible—seemingly with any diet rather than a vegetable diet. He had tried quinin intravenously, without any benefit.

DR. WINFIELD said he had seen a good many cases in the last few years and had tried arsphenamin, but thought it made the patients worse. So far as a vegetable diet was concerned, he agreed with Dr. Highman. The patient should be well nourished.

Dr. Winfield said he had tried Fowler's solution in large doses, but without any benefit, and he had known of one patient who recovered under auto-serum treatment.

DR. KINGSBURY said he had never seen any benefit derived from arsenic in a frank case of pemphigus. The patient Dr. Clark had shown had undoubtedly improved physically under the medication administered.

DR. BECHET said he had been looking up the question of prognosis in some of the recent textbooks, and had been struck by the favorable views taken by some of the authors. He had been under the impression that a well developed case of pemphigus with extensive involvement of the oral mucous membrane ultimately proved fatal. He would appreciate an expression of opinion on the part of those present on this interesting subject.

DR. CLARK said he had worked with this case along the lines mentioned by the members. Some one had spoken of the necessity of nourishing these patients. He had tried that for a long time, and the woman was losing weight and her mouth was doing badly; she could not take arsenic well, and was having a good deal of indigestion. She made no gain in weight until meat was eliminated from the diet, and then indigestion ceased. With the use of acetate of potassium and rhubarb and soda after meals she had had no indigestion, had gained ten pounds, and was able to take reasonably large doses of arsenic; her mouth was also better. She was put on an absolute vegetable diet. This was his first experience with such a diet in pemphigus.

DR. G. H. FOX said that with regard to arsenic in general, he had long ago made up his mind that while it was able to produce the most brilliant results in some cases, as usually administered, it had a bad effect in about nine cases out of ten. Nothing had caused him to lose confidence in Jonathan Hutchinson so much as his assertion that arsenic was a specific for pemphigus. He himself had rarely, if ever, seen any benefit that could not be attributed to the natural course of the disease; time after time he had seen arsenic administered without the slightest effect in controlling the eruption of the bullae. He had often wished that there could be a law preventing the ordinary medical practitioner from using arsenic in every case of skin disease. The patients would be far better off.

DERMATITIS VENENATA OF THE HANDS FROM HAIR DYE.

Presented by DR. HOWARD FOX.

L. G., aged 42, married, a colored woman (octoroon) born in the United States, six days ago had assisted a friend in dyeing her hair with one of the well-known commercial hair dyes sold in two separate bottles. Her hands, which had been in contact with the solution for about three-quarters of an hour, became stained, though she was able to remove most of the stain immediately by the use of hydrogen peroxid. On the following day the eruption appeared. This consisted of a swelling of the hands, particularly of the fingers, and a profuse eruption of pinhead to pea-sized, mostly unruptured, vesicles. The fingers were tender to the touch, and the patient complained of severe burning which interfered with her sleep.

DISCUSSION

DR. LANE said that such cases had been reported by barbers by several French observers, and that a number of years ago Dr. Fordyce had reported a case in a barber and had published a photograph of the affected hands.¹

DR. G. H. FOX told of an interesting instance of a man who some years ago used a well-known hair restorer, and who had a dermatitis or eruption on his scalp. He wrote to the manufacturer about it, and was told the preparation was harmless, that he could wash his hands in it, and it would do no harm. He tried this and almost immediately after spots developed on his cheeks and on the backs of his hands. Later he brought suit against the company. Their lawyer had consulted the speaker, and on request brought the patient for an examination. There were white spots on his hands and cheeks and neck. A few spots of vitiligo had accidentally developed about the time

1. Fordyce: J. A. M. A. 59:2043. 1912.

he used the hair restorer. The patient, an intelligent man, thereupon withdrew his suit. Before a jury these facts would have had considerable weight in establishing a claim of cause and effect.

SECONDARY SYPHILIS WITH LESIONS INDISTINGUISHABLE FROM PITYRIASIS ROSEA. Presented by DR. HOWARD FOX.

L. R., aged 15, a full blooded negress, born in the United States, about ten weeks ago noticed a genital sore, followed in a week or so by enlargement of the inguinal glands. About four weeks after the appearance of the genital lesions she noticed enlargements of the posterior cervical glands. About two weeks ago she noticed an eruption on the left arm which had gradually increased in extent. She complained of considerable itching, though she stated she did not scratch the skin.

On examination she presented typical hard enlargements of the inguinal, cubital and posterior cervical glands, numerous flat condylomas about the vulva and anus, and lesions of the tonsils which resembled mucous patches. The Wassermann reaction was strongly positive. The eruption consisted of superficial, partly discrete and partly confluent grayish patches with branny scaling and no evidences of scratching. It was situated on the trunk, neck and arms. It was indistinguishable from a classic pityriasis rosea, all of the types being present including punctate, fusiform and circinate macules. There was no eruption on the face.

DISCUSSION

DR. G. H. FOX said that if a few injections caused the eruption to disappear quickly, he would think it was syphilitic, occurring as it did about the time a secondary eruption would be expected; but if it persisted for six or eight weeks in spite of the injections it would seem more likely to be a case of pityriasis rosea.

DR. TRIMBLE said that if he did not know the syphilitic history, he would make a diagnosis of pityriasis rosea.

DR. WISE said it was pityriasis rosea.

DR. CLARK said it was difficult for him to make a diagnosis of skin lesions in a negro. He was sure he had seen pityriasis rosea that resembled this case very much, but he could not make a positive diagnosis of pityriasis rosea. Dr. G. H. FOX had summed up the situation reasonably: if the eruption should disappear after injections of arsphenamin, all would agree that it was a secondary syphilitic eruption.

DR. HIGHMAN thought it was pityriasis rosea. It was not surprising that a negress should have some condition besides syphilis. The therapeutic test, as outlined by Dr. G. H. FOX, would clear up the problem. He had, however, recently seen a case of pityriasis rosea that cleared up rapidly in thirteen days; it was about ten days old when he first saw it, so that the total course was about three weeks. If a therapeutic diagnostic test for syphilis had been made in this case nothing would have been proved.

DR. HOWARD FOX called attention to a case recently shown at another meeting (not reported) in which an undoubted pityriasis rosea existed simultaneously with an initial lesion. In this case the sequence of events proved that the two diseases were present as a coincidence. In his case, the eruption which seemed a typical pityriasis rosea, had appeared at a time when a secondary

eruption of syphilis might well have been present. This he thought of interest on account of the close similarity at times of the macular syphilid and pityriasis rosea. The eruption in this case did not resemble in any way the circinate syphilid that is so characteristic of the negro, the face, where this manifestation was usually present, being entirely free.

SARCOID OF BOECK? Presented by DR. HOWARD FOX.

E. G., 31 years old, a full blooded negress, born in the West Indies, a domestic, had first noticed a lesion on her nose five months previously. This had gradually increased in area, and now appeared as a round, smooth, purplish, fairly sharply bordered patch, the size of a nickel, situated on the lower half of the nose. It did not give rise to any subjective symptoms. It was somewhat infiltrated and slightly elevated at one point. The skin of the entire nose was unusually oily and the follicles patulous. She was a well nourished, robust appearing woman, in apparent good health. She presented no symptoms suggestive of leprosy.

DISCUSSION

DR. WISE said the case interested him very much because he had in private practice a young negro woman from the Island of Barbados with exactly the same type of lesion. A biopsy had never been made. Whether or not it was a case of sarcoid, he could not say, but that seemed the nearest diagnosis one could make. A diagnosis of lupus erythematosus might be made, but there was no scaling. Without a biopsy the diagnosis was difficult.

DR. BECHET thought the diagnosis of lupus erythematosus should be entertained. The follicles in the center of the lesion were prominent and patulous. Slight scarring seemed to be present.

DR. LANE said he could discover none of the characteristics of lupus erythematosus in the lesion. The pores were somewhat enlarged but otherwise the epidermis appeared normal. Without the history he would have made a diagnosis of pigmented nevus. The lesion was soft, slightly elevated, and covered with normal skin. If not a nevus, it was probably a sarcoid of Boeck.

DR. CLARK was inclined to think it might be a case of sarcoid in the declining stage. He had seen cases of sarcoid disappear apparently without leaving any scar tissue or atrophy, and this might be such a case.

DR. HOWARD FOX said opinion had been divided as he had expected it to be between sarcoid of Boeck and lupus erythematosus. It was not feasible to excise a piece of tissue from the nose, and the diagnosis would probably remain unsettled. He intended to try the effect of the Kromayer lamp with pressure.

MULTIPLE SEBACEOUS CYSTS OF THREE YEARS' DURATION

Presented by DR. WISE for DR. FORDYCE.

J. C., aged 34, presented innumerable barley-corn to split-pea sized, soft, hemispherical tumors on the trunk; interspersed among these were many comedones. The lesions were grouped chiefly about the anterior axillary fold and on the chest and upper abdomen. A biopsy confirmed the diagnosis.

FURTHER REPORT OF DERMATITIS VENENATA FROM CASHEW NUT. DR. HOWARD FOX.

Miss M. L., a laboratory worker in the Department of Agriculture, suffered a severe dermatitis venenata in September, 1920, after handling oriental

cashew nuts.² On this occasion, during the handling of the cashew nuts, her hands had been stained black by the juice, which is a well-known cutaneous irritant. On Feb. 4, 1921, in preparation of a thesis on the nuts which had apparently caused her dermatitis, she again made microscopic sections, but used special precautions against further irritation. The nuts were opened by another worker in the laboratory and she handled the fragments with forceps and also wore rubber gloves. During her work, for about three hours, a piece of the shell lay on the table within a few feet of her microscope. Immediately behind her was an open pail, with no water, containing a half dozen shells of nuts that had been opened. On the same evening, as a supposed precaution, she had used some zinc ointment on her face. On the following morning the eruption appeared first on the neck (where no ointment had been used) and later in the day, on the face. It consisted of redness, swelling, itching and slight vesiculation. At the end of two weeks it had disappeared entirely. There was no other apparent cause of the dermatitis except the irritation of the volatile fumes of the juice of the cashew nut to which she had apparently been sensitized. She had not been exposed to any other known irritant, such as hair lotions, etc., had not been in the country for six weeks previous to the present eruption and until February 4 had not worked in the laboratory for two months.

DR. WILLIAMS, referring to the interval after an exposure to poison ivy before the eruption develops, said that he remembered being exposed to ivy poisoning in the fall while trying to get out some dead vines. Three or four small vesicles appeared, but it was a week before the eruption amounted to anything at all.

DR. WISE said he had seen the patient's eruption, and had not thought of ivy poisoning. Her eruption of dermatitis venenata was much more dusky, and resembled more a mild chrysarobin dermatitis than that of poison ivy. When he saw the case it was a dusky edematous eruption, and he had no doubt that the nut alluded to and nothing else was the cause of the eruption.

ACUTE GENERALIZED PSORIASIS FOLLOWING INJECTIONS OF
ANTISTREPTOCOCCIC SERUM. CASE REPORT. Presented by
DR. HOWARD FOX.

G. M., 24 years of age, a married woman, born in the United States, for the past ten years had suffered from dry, scaly patches on both elbows, a condition which was said to have been psoriasis. About two months ago, she had an attack of "septic sore throat" for which she was given one subcutaneous injection of antistreptococcic serum. Following this injection the condition in the throat rapidly improved, but three days later a profuse eruption appeared suddenly on the greater part of the body, except the face, palms and soles.

When examined, after the eruption had been present for five weeks, she presented a typical example of punctate and guttate psoriasis, extensively distributed over the trunk and extremities. The scalp was also involved. The eruption occasioned a sensation of burning. Under treatment it had improved greatly during the past month.

DR. HIGHMAN inquired how long the patient had been ill with the sore throat before she received the streptococcus serum. He had seen psoriasis frequently after a febrile disease when no serums or the like had been used,

2. Arch. Dermat. & Syph. 3:202 (Feb.) 1921.

and wondered whether this was not due to the febrile reaction itself rather than to the injection. Many persons have acute psoriasis without having either fevers or receiving injections, and the latter probably had a coincidental rôle in the case reported.

DR. TRIMBLE, referring to the case of psoriasis, told of an instance in which two typical large psoriasis patches were limited to the elbows for years without an outbreak elsewhere. About ten years ago, when it became fashionable to wear short sleeves, the young woman thought she would like to get rid of the lesions, and was given chrysarobin ointment; immediately after the chrysarobin treatment, which started to clear up the patches, she had an outbreak of psoriasis all over the body, and has had it ever since.

DR. WINFIELD said that several years ago he had published in the *Journal of Cutaneous Diseases* a report of a series of psoriasis cases—some of them in children—in which the first attack of psoriasis followed a sore throat. This winter he had seen two cases—one in a child, the other in a woman of over 30, who developed an acute attack of psoriasis two weeks after a streptococcic sore throat. Neither patient had ever had psoriasis, nor was there any history of the disease in the family. Recently one of the patients reported some years ago had returned with a typical attack of psoriasis. He was inclined to believe that in many cases of psoriasis the first attack could be traced to some affection in the throat, and therefore thought that the cause of psoriasis, whatever it was, sometimes gained access to the system through the tonsils.

REPORTS ON CASES PREVIOUSLY PRESENTED.

DR. WILLIAMS said that of the two cases presented by him two months ago, one, a case of blastomycosis or possibly tuberculosis verrucosa cutis, had been shown at the Academy, and Dr. Pollitzer had suggested the possibility of syphilis. Arsphenamin had no effect on the patient, but after a second roentgen-ray exposure, the condition improved decidedly.

Another patient was presented the same evening with erythema bullosum or pemphigus. The man improved, and the skin healed, but on account of the poor circulation in the hands he was given iodid of potassium. The bullae reappeared. The iodid of potassium was stopped, and the skin rapidly approached normal, but he still had cold fingers.

Another case was that of a private patient who came for treatment about January 3. She had been in the country where poison ivy was plentiful, and she might have been exposed, though she had no knowledge of it. She had an acute vesicular bullous eruption on the hands and palms—a typical picture of a severe dyshidrosis. She also had small red papules or deep vesicles on the forearm. It seemed that it might be a possible case of epidermophyton infection, and she was given Whitfield's ointment, but it did no good. Two weeks later she was given soap and water and told to scrub hard and she reported that it disappeared within forty-eight hours after the scrubbing. After that Dr. Williams got a laboratory report of *Trychophyton asteroides* growing in pure culture from the roof of a vesicle taken at the first visit. Six weeks after the first visit, the skin was practically normal, except for a little dryness and scaling on the little finger, the spot where the eruption first appeared.

DR. CLARK reported the findings in a case of purpura hemorrhagica of the acute fulminating type. The patient presented himself after having had hemorrhages from the gums for five days. He went to his dentist who cleaned his

teeth, but he was not benefited. The day following he had punctate hemorrhages into the skin, and four days after the condition started he consulted the speaker with a history of dark colored stools and discolored urine. He was admitted to the hospital, and blood was found in the urine and dark colored stools. The gingival mucous membranes were bleeding, so that it was almost impossible for him to sleep owing to blood trickling down his throat. The patient looked as though he had lost considerable blood, and he had an evening temperature of 100.5. During the next five days he received 200 c.c. of horse serum. His temperature began to rise, so that it was thought he was having a serum sickness from the horse serum rather than anaphylaxis.

While the horse serum had stopped the bleeding from the gums almost entirely, and the bleeding in the skin and bowels, he still had blood in the urine, and it was thought he ought to have more serum. He received a transfusion under a careful aseptic technic, but his temperature remained high, and it was evident that he was seriously ill. Directly after that a blood culture was made, and a pure culture of what seemed to be *Staphylococcus albus* was found. A second transfusion was made after forty-eight hours, but the patient died, with a temperature of 106.5 F.

Blood was again taken from this patient under careful aseptic technic at the time of the second transfusion, and a pure culture of *Staphylococcus albus* was found. These cultures have from generation to generation and with time distinctly changed, so that the pathologists had later considered that this might be called a *Staphylococcus aureus* infection rather than a *Staphylococcus albus* infection.

No focal infection could be found. The illness came on without apparent cause. Naturally the question has arisen, whether or not he was infected with the *Staphylococcus aureus* at the time of his first transfusion while in a depleted state or at the time of his injection with the horse serum.

DR. CLARK said that in so far as he knew, no such findings had ever been recorded in a case of purpura hemorrhagica.

DISCUSSION

DR. HIGHMAN said that sepsis often began with purpura, but that staphylogenic sepsis was rarer than streptogenic. On the other hand, in some purpuras a bacteremia rather than a true sepsis was seen. A differential blood count would have been desirable for purpura is one of the commonest precursors of leukemia. Often, in the later stages, one finds the staphylococcus or streptococcus as a secondary invader shortly before death. It did not seem probable that this man could have been infected by so careful a worker as Dr. Stetson, but more likely that he was septic from the start, having a cryptogenic infection.

DR. CLARK said the bacteria were slow in changing their color. They grew as ordinary white albus colonies, and changed in about ten days. He had recognized the truth of what Dr. Highman had said, that frequently there are purpuric lesions in sepsis, but this was a typical case of fulminating purpura hemorrhagica, beginning without any previous sepsis. The man had apparently been perfectly well, and the bleeding came on suddenly. When he presented himself he was well, except for the bleeding from the gums, the mucous membranes, and the intestinal tract and kidneys and into his skin. A mistake was made at the time in that orders were not carried out and cultures made at the first. When he received the second transfusion the culture that was

made at that time was the second culture. The blood picture at the time of admission showed no leukemic abnormality, a hemoglobin index of under 80, with three million red cells and a slight leukocytosis, with the normal percentage of polymorphonuclears to lymphocytes just about reversed.

FRED WISE, M.D., Secretary.

NEW YORK DERMATOLOGICAL SOCIETY

Regular Meeting, March 21, 1921

JAMES MCF. WINFIELD, M.D., *President*

CHRONIC ITCHING PAPULAR DISEASE OF THE AXILLAE (FOX-FORDYCE DISEASE). Presented by DR. HOWARD FOX.

Miss A. R., 20 years of age, a college student, born in the United States, first noticed an eruption in her axillae five years previously. On the entire area of the axillae, normally covered by hair, were numerous pinhead sized, firm, round, smooth, elevated reddish-yellowish, partly discrete and partly confluent papules. The eruption had always been attended with more or less itching. The disease was confined to the axillae, and the affected area was dry and devoid of hair. There was considerable pigmentation of the adjacent skin, due to recent roentgen-ray treatment. The patient was a brunette. She was a well nourished young woman, apparently in the best of health.

DISCUSSION

DR. LANE said that the roentgen rays seemed to offer the only hope of relief to these patients from the very annoying itching. None of the usual applications did any good. He had applied them all without any effect. There was great dilatation of the sweat glands and coils. It was difficult to say whether that was the result of the lichenified skin or whether the condition of the skin was the result of some toxic condition. Such cases were not limited to the axillae; they were sometimes seen about the pubic hairs and sometimes about the nipples.

DR. G. H. FOX agreed with Dr. Fordyce that the condition had something to do with the sweat glands that was entirely different from the ordinary lichenification of other parts. It was usually limited to the axillary and genital regions.

DR. BECHET asked Dr. Wise whether the lesions came under the classification of neurodermite, so accurately described by him in the *Journal of Cutaneous Diseases* in 1919.

DR. WISE replied that: most of the French writers included such lesions under the term neurodermite.

DR. TRIMBLE said he had seen many similar cases, and agreed with the diagnosis.

CASE FOR DIAGNOSIS. Presented by DR. TRIMBLE.

This case had been presented at the previous meeting for diagnosis, and was now presented with the biopsy report. M. C., a young man about 27 years

of age, an American, had a skin condition which had existed for one year. The locations chiefly affected were the shoulders, arms and forearms. There were also a few scattered lesions on the back. The individual lesion was a maculopapule, drop size, and of a distinct yellow color, slightly scaly and with no objective symptoms. There were a great number of these lesions situated close together, though always discrete. On the back and chest they were arranged in bunches or in groups; the infiltration in each lesion could be distinctly felt but not seen. The disease began on the neck and had slowly spread. The Wassermann reaction was negative; the urine examination was also negative except that there was a moderate excess of indican. The blood count was practically normal; blood sugar, 122 mg. to 100 c.c.

Pathologic Report: "Section shows a rather peculiar pathologic picture which is characterized by the following changes: There is a marked extracellular edema, which is in the upper part of the corium and continues into the adjacent epidermal structure above. In some places vesiculation appears imminent. In the epiderm there is found a peculiar hydropic degeneration of the 'prickle cells.' A cellular exudate is present in moderate amount, which is located around the hair follicles, blood vessels and sebaceous glands. This exudate consists chiefly of lymphocytes and plasma cells. The hair follicles are occluded with coreous plugs. There is also some moderate hyperkeratosis present. Unna's stain for mast cells, negative. Kresofuchsin stain for elastic tissue shows nothing significant. Diagnosis: Subacute inflammatory process."

DISCUSSION

DR. BECHET said he hesitated to express any opinion, but was inclined to think that the diagnosis of parapsoriasis should be considered.

DR. G. H. FOX said the case differed from any he had ever seen.

DR. LANE said that the histologic examination had disproved his diagnosis of urticaria pigmentosa, made on the first presentation of the patient. The case was still obscure, but parapsoriasis seemed to be the most probable diagnosis.

DR. WISE suggested that the microscopic slides should determine the case if compared with those from half a dozen other cases of parapsoriasis; if they belonged to the same class the slides should show some similarity. Dr. Trimble had not said it was not parapsoriasis, but had not been able to reach any definite conclusion. It would be interesting to make a comparison of the slides.

DR. TRIMBLE said the diagnosis was still in question, but he would be glad to follow out Dr. Wise's suggestion and compare the slides with others that had been identified. They had several specimens, though they were mostly of the papular type or the papular form of Juliusberg and the Brocq type of psoriasis in patches. If the case in question was parapsoriasis, then it would be the guttate type, and he did not think the Bellevue clinic possessed a specimen of that variety. He had seen only one other case, which had been shown at the Academy of Medicine several years previously.

LUPUS ERYTHEMATOSUS TREATED BY THE KROMAYER LAMP.

Presented by DR. HOWARD FOX.

Miss G., 59 years old, born in England, had previously been presented (*Jour. Cutan. Dis.* 1:714, 1920). She had been treated on an average of about once a month during the past year with the Kromayer lamp (distance treatment). As a result, the lesions on the chest (of a superficial type) had

entirely disappeared, while those on the face (more deeply infiltrated) had only been improved. The improvement after each treatment had seemed to be proportioned to the intensity of the reaction, the best results being obtained when vesiculation was produced.

DISCUSSION

DR. FORDYCE inquired whether Dr. Fox obtained results in the usual types of lupus erythematosus. He had been successful in curing several cases of lupus erythematosus of the fixed type by repeatedly curetting them, and following the curettage with tincture of iodine. In the majority of cases, recurrence took place, which should be treated in the same manner or by thorough cauterization with the galvano-cautery. By persistence in such treatment some patients could be cured permanently. He referred to one patient who developed severe catarrhal symptoms of the upper air passages whenever iodine was applied to the skin.

DR. G. H. FOX said he had once reported two or three cases of mild lupus erythematosus which he had cured with repeated applications of phenol; but in well developed cases he had never secured any perfect results except from curettage. He believed this treatment would cure nearly every case.

DR. BECHET told of a case seen in private practice in which the face, with the exception of the forehead, was completely covered with a superficial conglomerate patch of lupus erythematosus. Ninety-five per cent. phenol, thoroughly rubbed in with cotton swab, at intervals of two weeks, had within a comparatively short time reduced the lesion to half its original extent. Areas of healthy skin, several inches in diameter, appeared in the center of the diseased mass on the cheeks. The cosmetic results could not have been better. Unfortunately, the patient disappeared from observation before a complete cure could be effected.

DR. TRIMBLE said he had cured several rather stubborn cases and failed in others. He could confirm what Dr. Fox had said in regard to phenol. It was a very capricious disease; sometimes very simple remedies would cure a case, and at other times nothing would avail.

DR. G. H. FOX remarked that the late Dr. Allen used to lay great stress on using the curet—beginning from the healthy skin and working toward the center. When the central portion was merely scraped, the lesion was sure to return; but if care was taken to scrape from the healthy skin toward the center, better results would be secured.

DR. WISE said he would confine his remarks to the present case. The patient had had a very widespread, deep-seated lupus erythematosus when first treated, so that the result now exhibited was an excellent one, and the treatment was probably as good as any.

With regard to iodine: A woman had been treated at the clinic during the afternoon with a patch of lupus erythematosus on the scalp; every time iodine was applied a rash appeared all over her body, so that that treatment had to be abandoned and phenol substituted. It was rather unusual to see a case of iodism from a single application of iodine.

DR. HOWARD FOX thought that the quartz lamps produced the best results in lupus erythematosus when the patches were fairly superficial. For the deeply infiltrated lesions, he preferred flat applicators of radium (unscreened). Though he had had good results with radium, the frequent relapses and appearance of new lesions were discouraging.

KERATODERMA SYPHILITICA. Presented by DR. WISE for DR. FORDYCE.

F. L., 52 years of age, had been infected by her husband twenty-one years ago. Six years later, the present trouble began on the right foot, and for the past two years the left foot also had been affected. The heels showed marked involvement, with hyperkeratotic masses thinning laterally into individual verrucous lesions which extended upward nearly to the malleoli. A similar case was described by Baker in the *Journal of Cutaneous Diseases*, April, 1918, p. 220.

DISCUSSION

DR. TRIMBLE saw no special reason for thinking the condition was syphilitic. It was possible, of course, though he did not think that syphilis often caused such a clinical appearance.

DR. FORDYCE said it was unusual for syphilis to cause a lesion of this kind, although hyperkeratosis might develop on a preexisting keratotic condition. He did not think antisyphilitic treatment alone would cure it.

LICHEN PLANUS. Presented by DR. WISE for DR. FORDYCE.

M. K., a woman 48 years of age, presented a rather unusual eruption of three months' duration with a fairly general distribution. Pearly plaques appeared on the tongue, and about the left flank there was a definitely zosteriform arrangement of the lesions of lichen planus.

PIGMENTED NEVUS TREATED WITH THE KROMAYER LAMP.
Presented by DR. TRIMBLE.

A. B., a young woman 26 years old, was under treatment at the University and Bellevue Clinic. On the left side of the chest, just below the clavicle, there was a light brown nevus slightly larger than a silver dollar. About half of this lesion was exposed to the Kromayer lamp for forty minutes (pressure) on Feb. 26, 1921, with the usual reaction. Some of the redness following the Kromayer light treatment was still observable, although the pigment was entirely removed. The case was presented to show the result of treatment with the Kromayer lamp.

DISCUSSION

Several of the members expressed the opinion that the result was very good.

DR. BECHET said that while the result was an exceedingly good one, there was marked telangiectasia. Might it not be possible that the telangiectasia occurred more frequently after treatment of this particular type of lesion with radiotherapy or heliotherapy than after chemical cauterization? He might be mistaken in this premise, but he seemed to have observed such results.

DR. HOWARD FOX disagreed with Dr. Bechet's remarks about radiant energy. While it was well known that both roentgen rays and radium could produce telangiectases, the same was not true, so far as he was aware, of the quartz lamps. In fact, the quartz lamps constituted one of the best remedies for the removal of telangiectases, especially when extensive areas were involved.

DR. WISE said he had been much interested in the case and was surprised at what Dr. Bechet had said. He himself had never seen telangiectasis following the use of the quartz lamp. This patient showed only temporary inflammation. As Dr. Fox had said, one can certainly cure these conditions with the Kromayer lamp.

DR. TRIMBLE said that this was a very superficial pigmented nonhairy nevus, and it was evident that the Kromayer lamp would remove it. At his clinic, there was no fear in regard to the Kromayer lamp causing telangiectasis, although he had feared that perhaps all the pigment might be taken from the skin, leaving a white area like a spot of leukoderma instead of the normal skin. As for the use of chemicals, there was danger lest some of the strong acids might produce a keloid.

FIBROMAS OF THE VULVA. Presented by DR. HOWARD FOX.

F. C., 30 years old, a negress, born in the United States, married for the second time, first noticed the appearance of small tumors of the vulva two years previously. She presented one pedunculated, flattened, firm, small egg-sized tumor arising from the upper half of the right small labium. There were also two pedunculated tumors of chestnut and hazelnut size, respectively, arising from the upper portion of the small labium and the tissue surrounding the clitoris. They were firm to the touch, painless and were not lessened in size by compression.

ERYTHEMA INDURATUM. Presented by DR. WISE for DR. FORDYCE.

F. S., a woman 43 years of age, born in Austria, had been in this country for sixteen years. On both legs she presented involuting, nonulcerating nodules of several weeks' duration, firm and painless. The history and the Wassermann reaction were negative for syphilis.

CASE FOR DIAGNOSIS. Presented by DR. TRIMBLE for DR. MALONEY.

J. H., a white man, was born in Bulgaria thirty-four years ago, and had lived in England from the time he was 14 until nine years ago, when he came to the United States. For the past twenty years he had worked as a printer, with the exception of a period of about one year recently, during which time he sold fruit at an outdoor stand. With this exception, he had never been unduly exposed to the sun.

Fourteen years ago there appeared on the backs of both hands several reddish colored, pinhead-sized spots. Almost immediately thereafter, lesions of the same character appeared on his forehead and on one arm. These spots gradually increased in size until they reached their present dimensions "in a few years."

He presented thirty more or less round macular lesions on the forehead, each about one-eighth inch in diameter, reddish yellow in color and apparently pigmented; also fifteen similar lesions on the dorsum of each hand, and a few on the left arm. The lesions on the hands and arms were more irregular in outline and deeper red in color than those of the forehead. There were no subjective symptoms. Within the past month he had had a large area of tinea versicolor on his chest, which cleared up under treatment. Scrapings from the lesions of the forehead, arm and hands, when examined under the microscope, revealed no evidence of tinea.

CASE FOR DIAGNOSIS. Presented by DR. HOWARD FOX.

D. A., 17 years old, a negro, born in the West Indies, an elevator boy, three years previously suffered from an inguinal bubo, which had broken down and discharged for about a month. Since that time, there had been some perma-

nent enlargement of the inguinal glands, according to his statement. About one month ago he noticed two "pimples" on the sheath of the penis, attaining their present size at the end of two weeks. An interval of a day or two elapsed between the appearance of these lesions.

On examination, he presented two round, elevated, nickel-sized, button-like, hard, slightly tender lesions on the dorsal surface of the sheath of the penis. The overlying skin was dull reddish in color, dry, scaly, with no evidence of itching. In both inguinal regions there were visibly enlarged pockets of hard painless, separate glands. There was a small jagged scar in the left inguinal region, the result of the former ulceration. There was one enlarged cervical and one cubital gland, but no other signs suggestive of syphilis. The result of the Wassermann reaction had not been reported.

DISCUSSION

DR. SCHWARTZ and DR. POTTER were inclined to think the lesions were gummas.

DR. TRIMBLE said he had been trying to make up his mind as to whether they were two initial or two late lesions; he was rather more inclined to consider them initial lesions.

DR. FORDYCE did not think the lesions were the primary syphilitic lesions. He was rather inclined to regard them as gummatous.

DR. HOWARD FOX said there was no doubt that the lesions of the penis were decidedly hard on palpation. In this respect they resembled multiple initial lesions rather than gummas or cutaneous tuberculosis. It had been difficult to elicit an accurate history, and a positive diagnosis at present he thought could not be made.

DR. WINFIELD said that before the days of Wassermann one would have considered the case syphilitic. It seemed to be rather more usual for colored people to have enlarged glands than for white people.

PRURITUS WITH LICHENIFICATION AND NODULE FORMATION.

Presented by DR. WISE.

M. P., 50 years of age and of German birth, had come to Dr. Wise two months ago giving a history of having had "eczematous" attacks in various locations at intervals during the past twenty or twenty-five years, chiefly on the hands and feet, and usually with marked pruritus. The condition presented dated apparently from the summer of 1919, having at that time started from the vicinity of abrasions on the left hand. It rapidly became generalized, and at various times he consulted Drs. Fordyce, Berk and Lapowski. In his business he came into daily contact with raw furs, and thus arose the suspicion that he might have become sensitized to fur products. He had handled no dyes. His body presented a diffuse eczematous eruption with lichenification, accompanied by numerous small nodular formations on the trunk and extremities. The lymph nodes were enlarged, apparently as a result of absorption of toxic products caused partly by infection from constant scratching.

DISCUSSION

DR. HOWARD FOX thought it quite possible that the eruption had begun as an occupational dermatitis due to working in furs. He thought the pigmentation could be accounted for by prolonged scratching, and that it was not necessary for the patient to have taken any arsenic. The pigmentation, as well as

the thickened skin, was due to scratching. He did not think the eruption resembled mycosis fungoides, as some one had suggested before the patient was presented.

DR. KINGSBURY agreed with Dr. Fox in excluding mycosis fungoides. His first impression regarding the case was that the condition was due to the ingestion of arsenic, but the son also showed a great deal of pigmentation, so that arsenic could be ruled out. As for a fur dermatitis, one would hardly get such a condition from raw furs. If the furs were dyed, it would be another matter.

DR. TRIMBLE said he had seen a case very much like this one a number of years ago in Bellevue, and it was then called general lichenification. Dr. Williams had written it up in connection with a case of prurigo nodularis. He was inclined to think that arsenic had a good deal to do with the pigmentation and the enlarged follicles also. Of course, the itching and scratching might have caused a good deal of pigmentation, but the condition was so generalized and diffuse that it hardly seemed the man could have scratched himself over the whole integument.

DR. BECHET asked whether in his opinion a good deal of the pigmented-like appearance might not be due to a dirty skin. The patient might have neglected bathing for fear of the itching.

DR. G. H. FOX said he felt certain that if Hebra had seen the eruption he would have called it a chronic erythematopapular eczema—that was before the term lichenification was coined. If Duhring had seen it, he would have called it dermatitis herpetiformis. It presented all the earmarks of that disease. It was a chronic eruption occurring in a neurotic person in groups of papular vesicles, tending to get better until a new crop appeared, and it was extremely rebellious to treatment. Hot baths and inunctions of sulphur ointment would relieve, if not cure, the case.

DR. FORDYCE said he had seen this case two years ago, when it presented practically the same appearance as now. The diagnosis made then was generalized lichenification of the skin. He had been interested in this condition for a number of years, and had carefully observed a number of cases of it. He had also studied the condition histologically, and found that it showed a hyperplasia of all the layers of the skin, with an inflammatory reaction in the upper corium. There was no evidence of vesiculation nor other histologic findings of eczema. He had never seen such cases develop mycosis fungoides. It was difficult in this instance to determine the etiologic factor. He had, however, seen a patient with generalized lichenification who had had, since early childhood, recurring attacks of urticaria followed by the condition in question. This patient, after careful study, was found to be sensitized to egg white. Any food containing eggs was always followed by an attack of urticaria and by an aggravation of the existing lichenification. In Dr. Wise's case, the possibility of a sensitization to fur should be kept in mind.

GENERALIZED ERYTHRODERMIA WITH LICHENIFICATION. Presented by DR. WISE.

M. P., Junior, 16 years of age and American born, had been for the past two months under Dr. Wise's care. His complaint was an intensely pruritic generalized eruption of three months' duration. At first it was strongly suggestive of scabies, but this possibility was soon excluded. With his father,

he had been daily exposed to raw furs while at work, and the fact that both father and son were affected was strongly suggestive of a common cause for their trouble, which might be of occupational origin.

In reply to an inquiry as to whether the father had taken arsenic, Dr. Wise said that he had taken it for a short period, but had not continued to take it and had not taken it long enough to cause pigmentation. He had been using carboneol on his skin and had refrained from taking any prolonged baths to get rid of the deposit. Most of the coloring matter was probably either natural or was due to the carboneol.

With regard to the fur dermatitis as a cause to be considered, it would be difficult to discover whether there was any kind of inoculation, especially in the father, as there was no normal skin to try it out on. There was great cause for suspicion since both father and son worked in the same shop and both had a dermatitis of this kind, but it was difficult to prove it without further investigation.

EPITHELIOMA OF THE PALATE. Presented by DR. WISE for DR. FORDYCE.

A. B., an American sailor of 60, presented at the junction of the hard and soft palates and just to the left of the medial line, an ulcer of five weeks' duration. The lesion was circular and was about 1 cm. in diameter, with a raised edge and an irregular ulcerated base. There was no pain or emaciation, and no lymph nodes were palpable.

CASE FOR DIAGNOSIS. Presented by DR. WISE for DR. FORDYCE.

An actor, 42 years of age, gave a history of having had a recurrent bullous eruption for months for the past six years, the mouth, the feet, knees, hands and elbows being affected. The lingual, buccal and gingival mucosae presented bullous lesions, and there was one on the shaft of the penis. Dermographism was present. Food tests had been made, with unsatisfactory results.

DISCUSSION

DR. TRIMBLE said he had had a similar case with lesions that came back in the mouth, and he called it pemphigus.

DR. WISE said he had suggested the possibility of pemphigus, and that antipyrin had also to be considered—that and phenolphthalein caused bullae in the mouth and sometimes eruptions on the skin. Apolant had described excoriated eruptions in the mouth. This patient did not seem to have a normal mentality, and though he denied having taken any medicine, he admitted that he took a combined cascara tablet, which might have contained phenolphthalein.

KERATODERMIA OF THE PALMS. Presented by DR. WISE for DR. FORDYCE.

G. S., a German-born man of 47 years, had lately done veneering in a piano factory. For the past six months his hands, feet and legs had presented a scaling dermatitis, the palms being hyperkeratotic and painfully fissured.

DISCUSSION

DR. TRIMBLE was inclined to consider the condition an occupational disease. Some one suggested ringworm infection.

DR. FORDYCE said he had never seen ringworm produce such an extensive keratoderma, but that that ought to be considered.

DR. WISE said he thought it was an occupational dermatitis, but that the man used his right hand almost exclusively for his work, and that his left hand did not come in contact with the material used. Filtered roentgen-ray treatment would be tried on the case.

NEW YORK ACADEMY OF MEDICINE, SECTION ON DERMATOLOGY AND SYPHILIS

March 1, 1921

HOWARD FOX, M.D., *Chairman*

CARCINOMA EN CUIRASSE. Presented by DR. MITCHELL.

A married woman, 30 years of age, first seen on Feb. 10, 1921, gave the following history: She had an abscess of the right breast about 3 inches above her nipple in 1912, following pregnancy, for which she received surgical treatment. In April, 1919, she consulted a physician because of an indurated ulcer of the lip, a general reddish eruption and sore throat. Her blood at that time showed a + + + + Wasserman reaction. Since then she had received irregularly, weekly injections of mercury. In June, 1920, she felt a small lump in the scar of the abscess and was told it was probably a gumma; she was advised to continue with the injections of mercury. This lump grew rapidly, and she was advised in October, 1920, to have the breast removed, but refused operation. The lesion had spread rapidly, but did not cause much pain. On Feb. 10, 1921, a section was removed, and the report from the pathologist indicated carcinoma.

The lesion showed involvement of the right breast extending down on the abdomen and part way around the back, crossing the sternum in front and beginning on the left breast. The color ranged from pink in the newer part of the lesion to purple in the older parts. There were many dilated blood vessels and the skin was puckered, giving it the "orange skin" appearance. The patient was presented as a case of "cancer en cuirasse" in a woman with syphilis.

LICHEN PLANUS ANNULARIS. Presented by DR. CHARGIN.

Mrs. M. R. was 25 years of age. Her skin affection began about a year and a half previously on both knees. Later, the eruption spread to the rest of the body. At the time of presentation she showed lesions on the arms, legs, chest, abdomen and back. The lesions were of typical character, but the especially interesting point was the great number of annular lesions on the abdomen and back. These varied in size from that of a pea to that of a five-cent piece, and many were confluent, producing festooned figures. Many of the annular lesions showed within, and alongside of, their margin numerous keratotic plugs. The mucous membranes were not affected. Subjectively, the patient complained of considerable itching.

URTICARIA PIGMENTOSA. Presented by DR. CLARK.

M. M., aged 19, born in the United States, in domestic service, was under observation in Dr. Clark's service at the Skin and Cancer Hospital. The present eruption began on her shoulders a year previously and slowly spread in a scattered way to her chest, arms, thighs and legs, and had shown no tendency to disappear. The lesions themselves had not itched especially, but at times the patient had been troubled with more or less general itching or mild burning. She complained of having had several bilious attacks, and she suffered from chronic constipation. As presented, she exhibited on the areas mentioned in the foregoing dull red or brownish pigmented-looking, distinctly raised papules. She exhibited an urticarial condition on rubbing the skin and marked dermographism.

DISCUSSION

DR. ABRAMOWITZ inquired whether it was not unusual for urticaria pigmentosa to form a wheal when rubbed or traumatized. He had been unable to obtain this reaction on Dr. Clark's patient.

DR. CLARK replied that the patient had developed wheals on friction of the affected area.

DR. SCHEER said that he could confirm Dr. Clark's observation. He had rubbed one of the macules, and within a few minutes there was an elevation of about one-sixteenth inch at its site.

SYPHILIS (HEREDITARY) WITH PECULIAR BONE AND SKIN LESIONS. Presented by DR. CLARK.

R. J., a negress, aged 8, had had measles and whooping cough; otherwise, her adopted mother stated, she was well but seemed bad and irresponsible. Eight months previously the child had had some kind of an eruption, the lesions healing and new ones appearing at intervals. Recently it had been noticed that the elbows were stiff, and the child had trouble in dressing herself. The history was indefinite and unsatisfactory. As presented, the child showed scattered whitish scars on the body and extremities, and rather large parallel scars on her back with a tendency to keloid formation. Any of these skin lesions appeared as if they could have been traumatic, except for their general distribution. No active skin lesions were seen. Both elbows were almost completely ankylosed, and there was thickening of the humeri for about half their length upward from the elbow joint. A pronounced thickening was also noticeable on the skull in the right frontal region, also thickening of the tibia. These bony thickenings were not tender, and the child had not complained of much pain in the elbows. Her pupillary and other reflexes seemed normal. She was mentally alert and showed no stigmas. Her Wassermann reaction was negative. Roentgen-ray plates of the humeri showed a condensation osteitis and periostitis, and indicated that the lesions were specific rather than tuberculous.

DISCUSSION

DR. OCHS said that the condition was more of a scrofuloderma, for the child had lesions on the chin as well as on the chest. It did not seem to him like inherited, or even acquired, syphilis. The lesions were scattered throughout, and there was no infiltration. On account of the glandular involvement, the lesions on the chin and the negative Wassermann reaction, the child impressed him as having scrofuloderma rather than syphilis.

XERODERMA PIGMENTOSUM. Presented by DR. CLARK.

M. D., an Italian girl aged 3, began to have a freckled-like condition with a sunburned appearance of her face seven months after birth. These lesions grew more pronounced and also appeared on the child's neck. Later, areas of the lesions grew scaly and crusty, and recently superficial ulcerations had appeared on the child's cheeks and her eyes became sore.

As presented, the child showed a typical and advanced condition of xeroderma pigmentosum, with freckles, keratoses, crusted lesions and superficial ulcerating epitheliomas. There was an ulceration on the left lower eyelid, and the child had a marked conjunctivitis of both eyes and photophobia.

DARIER'S DISEASE. Presented by DR. HOWARD FOX.

L. T., 28 years old, an Italian woman, had suffered from an extensive eruption of Darier's disease for the past twenty years. She had been previously presented on several occasions (*J. Cutan. Dis.* **29**:181-551, 1911). The disease had increased by extensive exacerbations, with intervening periods of comparatively little change. She had been treated with both the roentgen ray and radium in the past ten years. Large areas on the abdomen had been treated with the old and unmeasured technic of the roentgen ray, and certain patches of eruption had apparently been permanently removed. A moderate amount of telangiectasia had been produced. In spite of this, new lesions had recently developed on these areas. Lesions on the neck had been treated with unscreened radium, with apparent removal, though with considerably deforming telangiectasia. In this region also, a fresh crop of horny papules had recently made their appearance.

PAPULOSQUAMOUS SYPHILID WITH NO APPARENT INITIAL LESION. Presented by DR. HOWARD FOX.

A. D., 17 years old, a mulatto, born in Spain, presented a profuse generalized eruption of two months' duration. It consisted of discrete papules, a few of miliary type, others of scaling lenticular type, dull red and nonpruritic. Some of the lesions suggested lichen planus. There was a general adenopathy, but no evidence of any initial lesion was found. Coitus was denied. The Wassermann reaction was strongly positive.

PAPULONECROTIC TUBERCULID. Presented by DR. ABRAWOWITZ.

Hilda B., a colored woman, 34 years of age, was born in the British West Indies, had resided in the United States for the past sixteen years, and was under observation at the Vanderbilt clinic. She was married, but had never been pregnant. Two years previously she had had pneumonia followed by pleurisy, and since then she had been troubled with "colds." The duration of the skin trouble was eight months. There were pea-sized raised umbilical nodules, several of which were pustular, on the backs of her hands and fingers. The extensor aspects of the lower and upper extremities showed some smaller sized papules also with depressed centers, and a few with keloidal scarring. There was one crusted lesion on her right ear. A biopsy and a Wassermann test had been taken, but no report had yet been obtained. There were no definite signs of tuberculosis in her chest.

SCROFULODERMA. Presented by DR. HOWARD FOX.

F. T., 15 years old, a negress, born in the United States, first noticed painful swellings on the left side of her trunk two years previously. There was no family history of tuberculosis. She had from time to time expectorated blood, had lost weight during the past year, and had recently suffered from night sweats. She presented enlarged lymphatic glands in the lateral cervical and right supraclavicular regions and along the anterior axillary fold. Two of these were soft and fluctuating. On either side of the chest and on the left side of the neck were yellowish-green crusted lesions of irregular shape, one of them of rupial type. The individual enlargements had broken down and suppurated about six months after their initial appearance. The Wassermann reaction was negative; the von Pirquet test, positive.

CHEILITIS. Presented by DR. WILLIAMS.

Miss L. S., aged 35, an American, said that for the past twelve years there had been an eruption on the middle of the lower lip, sometimes with a thick heaped-up crust, sometimes an erosion with a little inflammatory reaction. For about four years there had been a similar eruption on the upper lip, but never so severe or so extensive as on the lower lip. The crust was a thick translucent yellow masslike dried serum. For the past twenty-five years she had had a seborrheic dermatitis of the face.

GRANULOMA PYOGENICUM. Presented by DR. CLARK.

A. V., a girl, aged 6, born in the United States, first noticed a small pimple on her right cheek, near the lower jaw, three months previously. The lesion had grown slowly until it was the size of a large split marble. It had never been moist or discharged any purulent matter. As presented, the child showed a rather light-red, distinctly raised sessile tumor, sharply margined, not in the least granular, and exhibiting numerous small blood vessels running from the periphery toward the center. The lesion was rounded, raised, a quarter to a half inch thick, and was quite firm though not actually hard to the touch.

DISCUSSION

DR. ABRAMOWITZ said the case did not strike him as being granuloma pyogenicum, but rather some form of angiosarcoma. The lesion was smooth, dry, and traversed by small vessels. It rose directly from the skin, without a pedicle or base.

DR. LANE said that he did not see how this lesion, which was covered with unbroken skin, could be classed as granuloma pyogenicum. This name was applied to a pedunculated granuloma projecting through an opening in the skin. It was possibly a hypodermal pyogenic infection, though in some respects it suggested a neoplasm.

DR. HIGHMAN said that the diagnoses to be considered were granuloma pyogenicum and sarcoma. In the event of its being a granuloma pyogenicum, observation alone would tell. A great many sarcomas, however, had the appearance of the lesion presented in this instance. The only way of determination would be by microscopic examination. Of course, there would be certain risks in this, and possibly it was best simply to treat the child as though she had sarcoma.

DR. HOWARD FOX said that the case seemed to have a slight similarity to the so-called button-like epithelioma. One would have had to consider this possibility more seriously if the patient had been an adult.

BROMODERMA. Presented by DR. CLARK.

S. W., a little girl, born in the United States, was under observation at the Skin and Cancer Hospital. She had had occasional convulsions for a number of years. Four months previously she began taking five teaspoonfuls of medicine each day, which promptly relieved her attacks. Two weeks ago pustules developed behind her right ear, followed by a similar lesion behind her left ear and lesions in her scalp. As presented, the child showed bromoderma-like lesions on her scalp and behind the left ear; behind the right ear was a large granulomatous-like mass the size of a lemon, pushing out the ear from the head and quite painful.

ACNE NECROTICA; TREATED WITH TUBERCULIN. Presented by DR. CLARK.

A. S., aged 39, a milliner, born in Roumania, had had acnitis of the face and head for a year and a half. The lesions were rather numerous and left rather pronounced and deforming scarring because of their size and multiplicity. The patient made no improvement under various methods of treatment, but began to improve promptly under tuberculin; after eight months of this treatment he showed no new lesions.

MORPHEA WITH LEUKODERMA. Presented by DR. CLARK.

J. M., a schoolboy, aged 15, born in the United States, first noticed a whitish patch beneath his right eye about a year previously. A little later the patient noticed a whitening of the skin on the inner half of the right eyelid and eyebrow, and about that time some whitish spots appeared on the upper lip near the median line. As presented, he exhibited a typical yellowish, white, waxy hard band of skin extending from the nose and beneath the eye, while the inner half of the upper lid and eyebrow showed an equally typical leukoderma. There were several small spots of leukoderma on his upper lip.

FOLLICULITIS DECALVANS. Presented by DR. HOWARD FOX.

J. J. R., salesman, born in Russia, came to the United States nine years ago. A year or two later the disease of the scalp was first noticed. He was certain that it had not existed when he was in Russia. He presented numerous small, partially bald and coalescing areas scattered over the vertex, the largest area being the size of a dime. They were whitish, smooth, thickened, and the hair was somewhat coarse. There were no crusts, and no fungus was found on microscopic examination.

RAYNAUD'S DISEASE. Presented by DR. WILLIAMS.

Miss J. McK., aged 53, said that her trouble first started in the left index finger three years ago. This finger, without any apparent cause, became blue and cold at the tip, and the coldness spread farther up the finger, and later involved all the other fingers. When shown, all the fingers were blue and

cold, and the skin around them was very tight. The patient had been under observation for three weeks, and had been given arsenic by mouth with no apparent result up to date.

LYMPHANGIOMA OF TONGUE. Presented by DR. CLARK.

H. S., a girl aged 16, born in the United States, first noticed a small spot on the upper surface of her tongue near its center, five years ago. She described it as a bluish-white mark, such as might be left from an indelible pencil. The lesion slowly increased in size from time to time rather than gradually, and from time to time it would become perceptibly darker, remaining so for two or three weeks, when it would lighten up again.

As presented, the patient showed a rather flat circumscribed lesion on the tongue, about the size of a peanut, the posterior end of which gave a rather warty appearance, while the anterior half presented a group of translucent shining vesicles with a few black or brownish periods scattered around them like pepper grounds. The whole lesion was distinctly raised.

DISCUSSION

DR. HIGHMAN asked why any diagnosis was made. Why lymphangioma? It looked like a papilloma. In his opinion, the case should be presented without any diagnosis until an anatomic examination could be made.

DR. LEVIN said the case impressed him as being lymphangioma circumscriptum. It was situated on the dorsum of the tongue which was one of the common sites for the occurrence of this condition. The whole lesion was an elevated papillary growth on which there were grouped tubercular lesions, some of which appeared to contain fluid.

DR. CLARK said that in the daylight one could see at the lower end of the lesion typical small transparent vesicles grouped, with scattered small reddish dots, like pepper granules. When seen in daylight the condition was without question lymphangioma.

TUBERCULOSIS OF THE NOSE AND UPPER LIP. TUBERCULOUS ULCERATIONS OF THE PHARYNX AND THE UVULA. Presented by DR. MAX SCHEER.

W. J., aged 24, colored, born in the United States, single, presented himself at the Vanderbilt clinic on February 16, in the service of Professor Fordyce. He gave a history of a genital sore two years previously, which was followed by a sore throat but no skin eruption. At that time he received one injection of arsphenamin. During the past four months he had received one arsphenamin treatment and mercury by injection three times a week.

The trouble for which he was presented began four months ago, with pain in the throat and lesions on the upper lip and nose. The uvula and pharynx presented a few small nodules, and also a few small painful ulcers of irregular outline. The skin lesions were situated on the upper lip and lower half of the nose. The entire area appeared lobulated and violaceous in color, and consisted of nodules which had coalesced and ulcerated.

The histologic examination showed marked acanthosis which had resulted in a verrucous formation. In the derma there was tissue of a characteristic tuberculous structure (giant, plasma and epithelioid cells in nodule formation), and a marked inflammatory reaction tissue (dilatation of vessels, edema, round and connective tissue cells).

METASTATIC CARCINOMAS OF THE SKIN FOLLOWING A MELANOMA OF THE MUCOUS MEMBRANE OF THE UPPER JAW. Presented by DR. CLARK.

S. M., aged 40, a laborer, born in Poland, was operated on in October, 1920, for a black tumor of the gum, in the region of the lateral incisor and canine teeth. A few days later, an operation was performed on the right side of his neck for enlarged glands. One month later, glands were removed from the left side of the patient's neck. Three weeks ago the patient first noticed in the skin small nodular swellings scattered over the body and extremities. These swellings slowly enlarged until, when presented, some of them were the size of marbles; they had become slightly red and seemed to be breaking through the surface. The patient also showed a melanoma, extending back from the site of the operation on the hard palate and on the gum of the upper jaw. Numerous marble-sized tumors could be felt, slightly tender and quite hard, deeply-seated in the skin of various parts of the body. His liver, spleen and other internal organs seemed normal, but his health seemed to be failing.

The pathologic examination of one of the tumors showed it to be carcinoma.

PSORIASIS. Presented by DR. WILLIAMS.

H. M., a man about 55 years old, said that twelve years ago a red scaly eruption appeared on his back, which spread in patches to various parts of his body, at times improving and disappearing in places. He had a typical psoriasis when shown. Attention was directed to peculiar quadrilateral lesions with parallel sides on the buttocks, and to the peculiar distribution, one side of the body being much more involved than the other.

ERYTHEMA INDURATUM, HEALING UNDER TUBERCULIN. Presented by DR. CLARK.

N. S., 20 years of age, of Jewish origin, and a skirtmaker, began to have typical lesions of erythema induratum in his right lower leg three years ago. His left leg was markedly atrophied and had never shown any lesions. The lesions developed and healed, leaving adherent scars, and new lesions appeared quite regularly. Practically all the recognized tonic and hygienic measures had been employed, together with various local applications, during more than a year, but the patient's condition seemed to be uninfluenced until tuberculin injections were instituted about six months previously, since which time he had slowly improved, and no new lesions had appeared for some time.

DR. CLARK said that this was another case in which no improvement was made until tuberculin treatment was started. In his experience tuberculin was very effective for treatment of tuberculids.

ACRODERMATITIS CHRONICA ATROPHICANS. Presented by DR. CLARK.

V. K., a tailor from Russia, aged 26 years, first noticed a whitening of the skin of the left elbow region two years previously. A little later, a similar condition was noticed on the back of the left hand. These lesions became slowly more noticeable and increased in size, but were not attended with any discomfort. As presented, the patient showed waxy, whitish transparent atrophic patches about the size of the palm, with vessels showing through prominently. There were no signs of infiltration.

ACRODERMATITIS CHRONICA ATROPHICANS. Presented by Dr. WILLIAMS.

A. C., from Dr. Williams' clinic, a woman 39 years of age, an Austrian by birth, had been married seventeen years and had one child. The duration of her illness was eight months. She was not certain of the sequence of the skin changes. The lower part of the body, from the iliac crests to the metatarsal region, was involved. The number of elements presented were such as to give the suggestion of xeroderma in some areas, with faint depressed macules interspersed on a reddened skin. There was a distinct sense of infiltration which suggested scleroderma. This character was marked at the upper limit and along the tibiae. The toes were free from lesions, and were not sclerodermatous. Two triangular areas in the groin with one side of the triangle formed along Poupart's ligament and another side by the inner limit of the thigh were entirely free of lesions and approximated normal skin. The triangle on the left side was much more marked than that of the right side. There were no other skin lesions on the patient. The absence of anetodermia did not entirely exclude the diagnosis as it might be that the duration was not sufficiently long to permit the formation of this character of the disease. The patient had recently been presented before the Clinical Society of the Skin and Cancer Hospital, where the sclerodermatous changes were thought worthy of much consideration.

DISCUSSION

Dr. SCHEER said it was doubtful whether the primary condition was acrodermatitis. There was such an extensive scleroderma of the foot and thigh that the acrodermatitis might be secondary. The patient did not show an erythroderma, which was one of the cogent features of acrodermatitis chronica atrophicans. Scleroderma seemed the more probable diagnosis.

Dr. CLARK agreed with Dr. Scheer that scleroderma seemed the more probable diagnosis. the lesions near the groin showing decided scleroderma.

Dr. ROSTENBERG thought it was acrodermatitis of not very long standing. The same patient had come six or eight months previously to the Lenox Hill Hospital Dispensary, presenting a classic picture of acrodermatitis atrophicans with sharp demarcation of the process on the buttocks and atrophy over both knees. He thought that if the case was observed a little longer anetodermia would develop and the diagnosis would be verified.

CASE FOR DIAGNOSIS. Presented by Dr. CLARK.

J. K., a waiter of German extraction, aged 38 years, first began to have superficial slightly scabby lesions on the arms and trunk eight months previously. New lesions slowly developed, and the patient thought that none of the lesions had disappeared. As presented, numerous lesions were seen on the arms and body, varying in size up to a large thumbnail. Some of the lesions in the region of the elbow showed distinct scaling, were slightly infiltrated, and were suggestive of psoriasis, though they did not show minute bleeding veins when the scale was scratched off. The lesions on the body were not infiltrated, had few or no scales, and rather resembled a parapsoriasis guttata. A hurried biopsy report seemed to deny a psoriasis or lichen planus. A further report of the biopsy would be submitted later.

DISCUSSION

DR. HIGHMAN said that as the lesions appeared at night it would be impossible to say what the condition was. The location on the upper extremities, the presence of a few papules on the knees and the thighs, together with the lesions on the buttocks and the small of the back and other lesions over the body, suggested a fading psoriasis. In addition to that there was the distinct grouping of the lesions along a scratch on the left arm, like either psoriasis or lichen planus. In his opinion it was an acute psoriasis, now waning.

DR. CLARK said he had received the biopsy report over the telephone, which said positively not psoriasis or lichen planus.

DR. HIGHMAN replied that a negative anatomic report on psoriasis was valueless. In the first place, the biopsy might have been made from a lesion without any marked attributes; in the second place, the lesion might have been involuting when the examination was made, which would give an indeterminate microscopic picture. Of course, in the involuting stage of lichen planus there were more signs of the disease microscopically, and there the microscopic findings were of value. The microscopic diagnosis of parapsoriasis was not of much value.

MULTIPLE KELOIDS. Presented by DR. CHARGIN.

E. L., from Dr. Goldenberg's service at Mount Sinai, 17 years of age, single, and a mechanic's helper, two years prior to presentation had developed acne of the indurated type which at the onset was limited to the back, but which later affected the face as well. The eruption was treated mechanically with some form of cutaneous punch. Following this treatment keloids began making their appearance at the site of the former acne lesions. At the time of presentation, more than 300 keloids were scattered over the back, upper arms, neck and upper legs. The face was singularly free of keloids, although the patient showed numerous scars; he had received the same treatment on the face that was employed for the back. The keloids varied in size from that of a pea to irregular and confluent lesions 2 inches or more in length. At another institution he had received numerous roentgen-ray treatments, apparently without any benefit.

DR. CHARGIN stated that in view of some recent work reported in the literature, he had had the patient examined for evidences of hyperthyroidism, but this was not found.

SYRINGOCYSTOMA: RESULT OF ROENTGEN-RAY TREATMENT.

Presented by DR. HOWARD FOX.

E. W., 39 years old, a negress, born in the United States, had been presented previously (*J. Cutan. Dis.* **35**:238, 1917). She was again presented to show the result of treatment with roentgen rays, which had been applied on the right side of her chest and neck. As a result, the lesions on the chest had entirely disappeared, leaving a normal skin, which contrasted with the untreated side of the chest. She had been given, experimentally, ten roentgen-ray treatments of one-quarter Holzkecht unit (skin distance) five years ago. A small area of the left side of the chest had also been treated with an unscreened plaque of radium, with subsequent removal of the lesion, though a depigmented area of skin had remained.

DISCUSSION

DR. CLARK said he would like to confirm Dr. Fox's results by citing another case seen three years ago, which entirely cleared up.

DR. POLLITZER said that ten years ago Ormsby published an extensive case of syringomyoma which cleared up under roentgen-ray treatment.

NEVUS PIGMENTOSUS. Presented by DR. CLARK.

J. S., a young man, aged 19, born in the United States, first noticed a spotty discoloration in the left pectoral region about seven years prior to presentation. The patient was certain that the skin in that area was clear previous to that time.

The patient exhibited light brownish pigmented lesions irregularly distributed, showing intervening areas of normal skin. The lesions were not scaly, and an examination of scrapings was negative for *tinea versicolor*. The patient was presented because of his *tinea versicolor*-like appearance and history.

PSORIASIS OF THE PENIS. Presented by DR. OCHS.

D. W., 32 years old, a salesman, first noticed an eruption on the glans penis a year previously. This consisted of three rounded pea-sized, slightly elevated lesions covered with lightly adherent silvery scales. The latter were removed on bathing, leaving a reddened and glistening base. There had been no change in the eruption during the past year, and no cutaneous lesions had appeared on any other part of the body. Repeated Wassermann tests had been negative.

DISCUSSION

DR. G. H. FOX said that he hated to differ with the diagnosis. In this case he could not but admire the boldness of any one who would make a diagnosis of psoriasis based on a few scaly lesions on the penis without any eruption elsewhere. It seemed to him more likely to be a case of lichen planus than of psoriasis.

DR. POLLITZER agreed with Dr. Fox.

DR. LANE could not disprove the diagnosis, but thought that a positive diagnosis from two minute lesions on the glans was an impossibility.

DR. OCHS said that if it was lichen planus he would like to know why arsenic had not helped the condition, and also why lichen planus should exist primarily on the penis and not elsewhere—in the mouth, etc. This certainly was a unique case if it should prove to be lichen planus.

DR. POLLITZER said he had never seen psoriasis of the glans penis limited to that region, in fact it was not common in that region even in extensive psoriasis. He had, however, seen lichen planus limited to the glans penis.

DR. MITCHELL cited a case in which the lesions were situated primarily in the same region. A tentative diagnosis of psoriasis was made, and subsequent examination showed lesions on the leg which confirmed the diagnosis made on the penis. This man also might develop other lesions later.

DR. HOWARD FOX agreed with Dr. Pollitzer in regard to lichen planus. It was not a great rarity to see undoubted lesions of lichen planus, especially of the circinate type, appearing alone on the penis.

ANGIOMA SERPIGINOSUM. Presented by DR. OCHS.

M. P., 50 years old, born in the United States, was a married woman, the mother of two living children. The eruption first appeared six years previously on the back of the left hand as a small red spot about the size of a lentil, and quickly spread over the arm and shoulder. Soon new foci appeared on the upper part of both thighs and spread upward over the abdomen and downward to the toes, so that at the time of presentation the entire body, except the face and upper part of the neck, were involved. The lesions consisted of vascular macules showing characteristic "pepper grains." The color was generally bright red, except on the lower part of the legs, where it was decidedly bluish, the venous instead of the arterial capillaries evidently being involved. The macules on the lower part of the legs had a large center of normal skin, and radiating from these centers were the new blood vessels arranged as in the spokes of a wheel. The lesions had spread peripherally, the "cayenne pepper" spots coalescing, thus forming new blood vessels. A small portion of the body remained unaffected. There were no subjective symptoms except for a slight itching when the patient was very warm.

DISCUSSION

DR. OCHS said it seemed to him the patient was beginning to show lesions on the lower lip. The interesting feature in the case was not alone the extensiveness of the disease but the fact that the color had changed in the lower part of the leg. While all over the body there were arterial lesions, there was a venous condition on the leg.

DR. HIGHMAN said that the case was too interesting to be passed without discussion, and that Dr. Ochs was to be congratulated on being fortunate enough to present it before the Section. The lesions on the upper part of the body represented the classical picture of angioma serpiginosum; the lesions on the leg did not—and the case brought out prominently the curious ignorance that still exists regarding the entire group of capillary diseases. Five or six years ago Stokes published an article on telangiectasis due to syphilis, and perhaps some of the things grouped under this heading may be unique conditions. Of course if it were not for the lesions on the leg, it would be a clear case of angioma serpiginosum.

In regard to the treatment, it was possible that the experience of Dr. Howard Fox and Dr. Fred Wise with the Kromayer lamp and alpine light might justify trying these measures in this case.

DR. HOWARD FOX referred to a patient of Dr. Wise and one of his own who had responded in a most gratifying manner to treatment with the quartz lamps. The condition of Dr. Wise's patient had entirely cleared up at the end of a year or more, while the improvement in his own patient, when last seen, had been great. The best effects had been obtained after a severe bullous reaction.

DR. CLARK asked whether the light had been applied at a distance or by pressure.

DR. FOX replied that it had been applied at a distance.

DR. POLLITZER inquired about the Wassermann reaction.

DR. OCHS replied that the Wassermann reaction was negative.

PAUL E. BECHET, Secretary.

PHILADELPHIA DERMATOLOGICAL SOCIETY

*Regular Monthly Meeting, March 14, 1921*JAY F. SCHAMBERG, M.D., *Presiding*

PSORIASIS. Presented by Dr. WEIDMAN.

The patient, a white man, aged 33, had been under observation ten days. He had an outbreak of psoriasis with a seborrheiform distribution, the lesions being of guttate size. The case was presented to demonstrate linear lesions appearing along a scratch. There was a history of the patient receiving a scratch on the abdomen from a pin in his clothing and subsequently the disease developed along the scratch mark. The tar ointment with which the patient was treated had removed the scales, and the lesions were less conspicuous than when first seen. He was taking arsenic internally.

DISCUSSION

Dr. WEIDMAN added that he had seen lichen planus and warts develop along scratch marks but he had never noted it in psoriasis.

Dr. SCHAMBERG remarked that the condition was not infrequent. A few years ago he had conducted experiments along this line. Abrasions had been made in the skin and were inoculated with an emulsion of psoriatic scales. In a small proportion of cases linear psoriatic lesions developed. This was found to occur only during the evolutionary stage when new lesions were appearing. In the quiescent cases the experiment did not succeed. Photographs of these artificially produced lesions were published at that time.

Dr. CORSON said that judging by the appearance of the lesions in the case presented it was undoubtedly the type in which the inoculations had succeeded.

Dr. HIRSCHLER asked what effect arsenic had in these cases.

Dr. SCHAMBERG said that arsenic acted as a stimulant to the skin. In the inactive cases which required some stimulus to promote involution it often worked well. In those cases in which new lesions were appearing the stimulating effect caused an undesired activity in growth. This disease was the great dermatologic mystery. It had been known for 2,000 years and the etiology was still uncertain.

ICTHYOSIS HYSTRIX. Presented by Dr. BROWN.

A mulatto woman, 19 years of age, was a patient in the Maternity Department of the Philadelphia General Hospital (Blockley). She presented a congenital condition from which she was occasionally almost free, due to its exfoliation. The arms from the axillae to the wrists were almost completely covered with elevated, rough, shaggy epidermal thickening. The color was dark with grayish shading. Irregular lines of fissuring ran through the area, giving a corrugated appearance. In spite of the apparent roughness and dryness, there was present a velvety texture when the hand was passed over the patch. The lower extremities were similarly affected. Keratosis palmaris et plantaris was present. The face was free, but on the forehead below the hair line, at the temples and on the scalp was a slightly raised, jet black patch with an irregular, sharply defined border. It closely resembled the appear-

ance of tar smeared on the skin and had not the verrucous character of the eruption on the extremities. Elsewhere on the trunk the usual appearance of ichthyosis was noted, the lines of cleavage marked with great distinctness.

DISCUSSION

DR. SCHAMBERG said it was unusual to see that amount of epithelial hypertrophy. There was no doubt as to the correctness of the diagnosis.

LEUKEMIA CUTIS. Presented by DR. DENGLER.

The patient, an Italian laborer of middle age, was brought from the wards of the Hospital of the University. The present condition began six years ago as an erythematous eruption on the neck and shoulders. Eight months later the entire body was involved by gradual extension. Six months ago the cervical, axillary and inguinal glands became enlarged. At the time of presentation there was noted a universal scaly erythrodermia. The spleen was enlarged. The superficial lymph nodes, notably the inguinal groups, stood out in relief. The temperature was 100 degrees. Nodules had appeared in the skin at times but all had subsequently disappeared. Itching was intense and uncontrollable. The Wassermann reaction was negative. A leukocytosis of 42,000 existed with 58 per cent. lymphocytes. A biopsy had been made.

DISCUSSION

DR. SCHAMBERG called attention to the interesting picture presented. Such an eruption might occur in mycosis fungoides, leukemia cutis, pityriasis rubra of Hebra and Hodgkin's disease. The glandular and splenic enlargement and the blood picture indicated a hematopoietic origin. It was hard to differentiate the premycotic from the leukemic type of eruption. On account of the blood findings, the speaker thought the case one of leukemia cutis. It was generally accepted that the condition known as Hodgkin's disease could not pass into leukemia but mycosis fungoides could undergo leukemic transformation. Ehrlich and Pinkus believed that mycosis fungoides, Hodgkin's disease and leukemia were closely related and belong to the same group. The evidence here favored leukemia but repeated blood studies were necessary.

DR. KLAUDER suggested establishing the enlargement of the bronchial glands by roentgenogram thereby adding data for diagnosis.

DR. WEIDMAN said the sections made from the biopsy agreed neither with mycosis fungoides nor leukemia. Possibly this difficulty might be traced to the fact that the lesions excised were early ones. On that account it was necessary to hold the matter under advisement until further development of the disease. At the periphery of the lesions spindle cells continuous with those of the collagen bundles were noted; that is, there was present a transition from lymphocytes to spindle cells. At the margins of the infiltrate it shaded off and under the sound epidermis the lymphocytic infiltrate ceased entirely.

DR. SCHAMBERG concluded the discussion by adding that Douglas Simmers regarded the eruption as an effort to eliminate toxins through the skin. But in leukemia there was usually a leukemic infiltration of the skin. Roentgen-ray therapy was suggested for relief from the itching as well as a curative measure.

FOR DIAGNOSIS. Presented by DR. STRAUSS for DR. CORSON.

A white boy, aged 15 years, had a curious group of small pitted scars in front of the right ear. They had been present for eight years. Either the

patient and his family were unobservant or the primary lesions were inconspicuous for there was no history of their presence. The scars were from 2 to 5 mm. in diameter and were arranged in a vertical distribution, some fifty or sixty being present. There were comedones in some of the pits; otherwise the only active lesion was the topmost one which displayed a dry yellow crust with a darker, horny, acuminate center.

DISCUSSION

DR. SCHAMBERG thought the case was an unusual type of papulonecrotic tuberculid. There must have been a preceding inflammation unless the case was one of idiopathic atrophy.

LEISHMANIASIS. Presented by DR. KLAUDER for DR. SCHAMBERG.

A white man, aged 43 years, lived in South America for ten years, returning to the United States six years ago. Seven years ago the present eruption started on the left ear; six years ago on the right one. There was present a marginated, pinkish eruption on the lobule of each ear. The surface was crusted lightly. The area involved was about the same on both sides, the entire lobule and adjacent margins of the pinna being affected.

DISCUSSION

DR. SCHAMBERG said the case was one of leishmaniasis. The appearance shown was almost a replica of that seen in other patients affected with the disease. The organism had not been demonstrated, but the results of treatment corroborated the diagnosis. New superficial ulcers had recently formed with extension of the patch. Some of the lobule had been destroyed. The treatment had consisted of intravenous injections of 5 c.c. of a 1 per cent. solution of tartar emetic given every second day. In all, five injections had been given with decided improvement in the eruption. It was thought that the disease was due to infection by an insect. Attempts to inoculate guinea-pigs and a monkey from this case had failed. In this case there had never been deep lesions but superficial ulcerations covered with a crust. The similarity to recently reported cases suggested the diagnosis. Many cases were found in South America.

DR. WEIDMAN mentioned that Patton had shown the *cimex lectularius* to be a spreader of this disease.

DR. CORSON remarked that the case resembled lupus erythematosus, clinically.

DR. KLAUDER brought up as of interest the fact that Donovan bodies had been found in inguinal ulcerations.

DR. HIRSCHLER asked how the intravenous injections acted. Did they make the patient ill?

DR. SCHAMBERG replied that this patient did not feel sick after the treatments. Diplococci had been found associated with the bodies, but their significance had not been worked out.

DR. WEIDMAN said that to be considered causal bodies of proper morphology should be found in the lymphocytes.

DR. SCHAMBERG concluded the discussion by mentioning that in a recent number of *The Journal of the American Medical Association*, cases of inguinal granulomas had been reported. Possibly they were cases of leishmaniasis.

ADENOMA SEBACEUM. Presented by DR. KLAUDER for DR. GREENBAUM.

This patient and those in the two following cases were sent to the meeting by Dr. Greenbaum, who was unable to be present. The patient was an under-sized boy, 7 years of age. The small tumors on his face had been noted for several years past. The child was an epileptic. The tumors were scattered over the forehead, sides of the nose and upper cheeks. They were bright red, quite numerous and most of them were the size of a pinhead. A few telangiectases were noted in the affected region and an angioma on the forehead. There was no discussion as the diagnosis was plainly adenoma sebaceum.

LUPUS ERYTHEMATOSUS. Presented by DR. KLAUDER for DR. GREENBAUM.

A white woman, aged 29, presented an erythematous patch on the left cheek of three years' duration. On the dorsum of the fingers of the left hand, patches of a similar appearance had been present four or five weeks. The eruption was the vascular type of lupus erythematosus. It disappeared in winter and returned in the spring. On the tip of the nose and the right cheek there was a much fainter outbreak.

DISCUSSION

DR. SCHAMBERG warned that when the eruption of this disease spreads to parts other than the head the likelihood of a serious acute condition developing must be borne in mind. A patient of the speaker's had had high fever and a pneumonic consolidation lasting several weeks. In others an erysipeloid eruption of the face is succeeded by a pneumonic condition.

FOR DIAGNOSIS. Presented by DR. KLAUDER for DR. GREENBAUM.

A colored woman of middle age presented a few pigmented spots of ten years' duration. They were each about the size of a five-cent piece. One was on the wrist, others on the legs. There were ulcers in the center and distinct nodulation was apparent.

DISCUSSION

DR. SCHAMBERG suggested a circumscribed prurigo nodularis and a cutaneous response to scratching. He thought that in many cases of that disease the nodules are secondary to scratching. The name lichen obtusus was once used for such a condition.

DR. STRAUSS said that most of the cases described had occurred in women. In this case there had never been more than half a dozen lesions.

EDWARD F. CORSON, M.D., Secretary.

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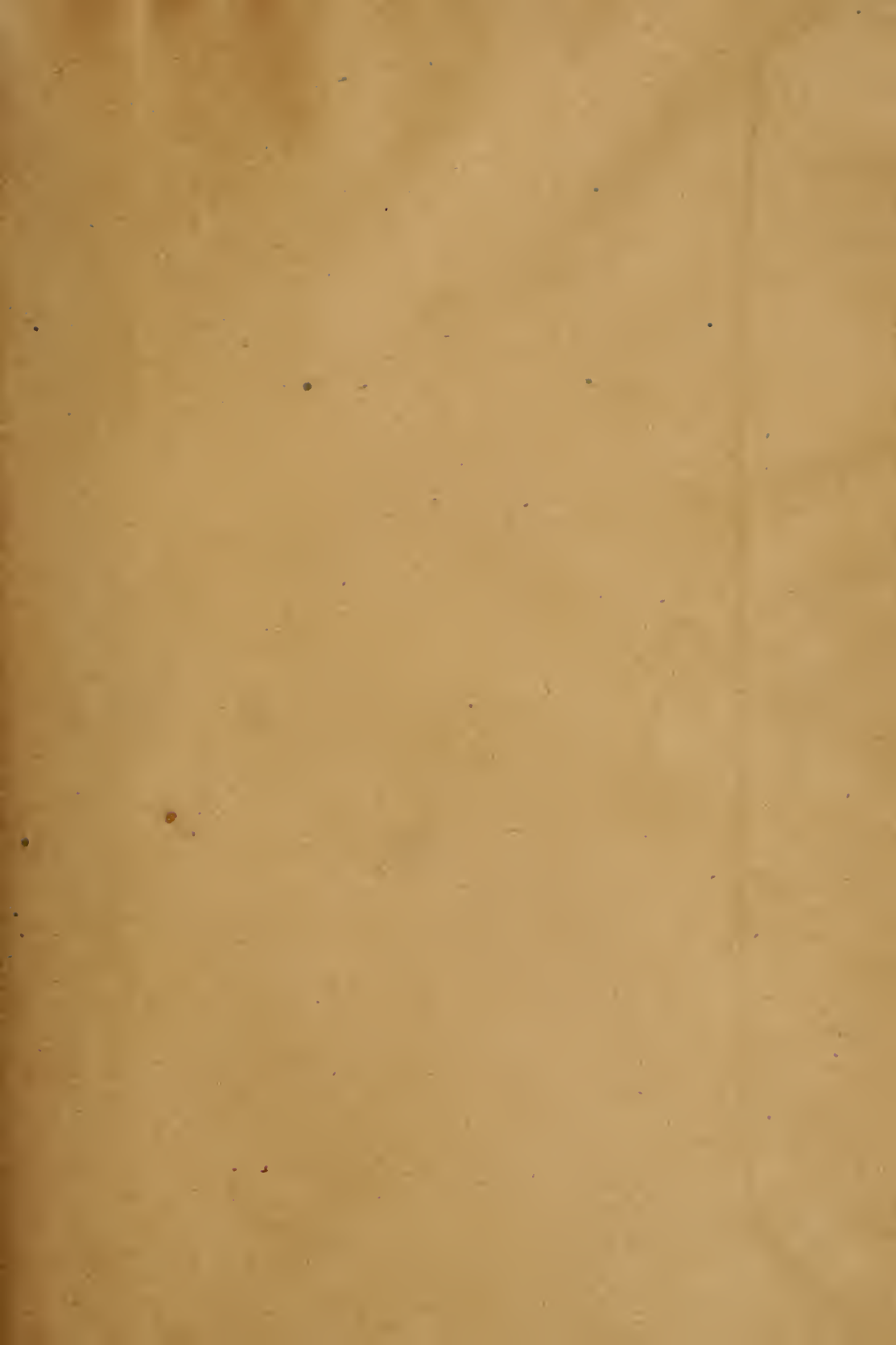
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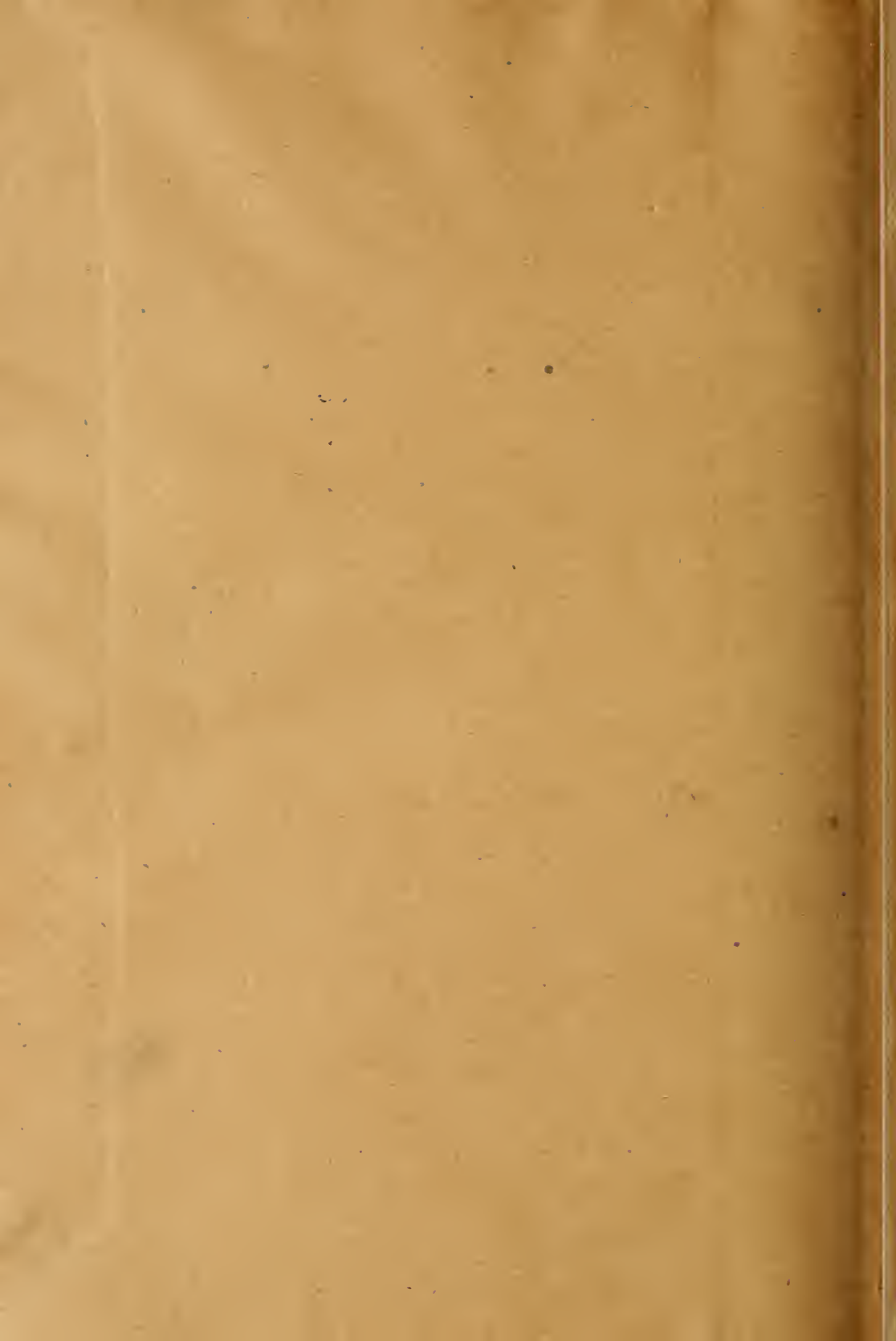
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